

# 1

## Epidemiology, etiology, and consequences of obesity

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### Learning Objectives

The reader will be able to:

- Define obesity in adults and children.
- Describe the estimated prevalence of obesity in adults and children in the United States and for adults, globally.
- Discuss how obesity prevalence is estimated in the United States.
- Discuss the health consequences of obesity with respect to diseases commonly associated with obesity, health-related quality of life, and premature death.
- Identify putative causal factors related to the development of obesity.

### Introduction

“Last week, I met with the G. family in the—clinic at my hospital. One of the parents was overweight, and the other was obese. The five children were more severely obese and had numerous weight-related complications—one had evidence of fatty liver, one had high blood pressure, two had gastroesophageal reflux, two had orthopedic problems, three had marked insulin resistance, four had dyslipidemia, and all had emotional problems related to their weight.

Sadly, this family might be a microcosm of 21st-century America: if we don't take steps to reverse course, the children of each successive generation seem destined to be fatter and sicker than their parents. How will obesity affect the physical and psychological well-being of children in coming decades? What effects will childhood obesity have on life expectancy, the national economy, and our society?”

D. Ludwig, *New England Journal of Medicine*, December 6, 2007 (1)

The above scenario typifies the great challenge of obesity in the 21st century—stemming the epidemic of obesity that threatens the health and quality of life of millions of people in all walks of life. Obesity is an increasingly

important problem in world health: its prevalence has greatly risen around the world in the last two decades; and it is affecting people of all ages and ethnicities, but some groups more than others, as will be discussed below. The onset of obesity is occurring at increasingly younger ages and its negative consequences are occurring earlier in life—a scenario with profound economic consequences as obesity becomes commonplace among the workforce. Obesity is affecting individuals in all social strata and it is escalating in the industrialized world as well as in developing countries. As the economies of developing countries begin to shift, and as peoples all over the world become more urbanized and make the transition from hard physical labor to intensive use of labor-saving technology, the incidence of obesity increases. Also, as food production and distribution systems modernize and as people's discretionary income increases, a wide variety of rich and highly palatable food is available to everyone. As a result, more people are overeating at a time when their energy expenditure is decreasing. Since fat storage occurs when the consumption of energy in food (i.e., calories, a measure of the chemical energy stored in food) exceeds energy expenditure (primarily, but not exclusively, through physical activity), these industrial, sociocultural, and economic

changes are shifting the energy balance, with the result that people worldwide are gaining weight.

This chapter presents current definitions of obesity, epidemiological data on the growing prevalence of obesity and its consequences, and a brief presentation of some of the putative causes of obesity, many of which will be developed in subsequent chapters. This chapter concludes with a brief discussion of obesity prevention, which is treated in depth in Chapters 24, 26, and 27, and of issues that merit further attention from the research community.

### Definitions and assessment

The human body contains essential lipids, for example, constituents of cell membranes, and also nonessential lipids in the form of stored triglycerides. These molecules are commonly referred to as “fat” but are technically referred to as “triacylglycerols.” They are stored in specialized cells called adipocytes (see Chapter 7 for more information on adipocytes). Obesity is simplistically thought of as the excess accumulation of stored fat, but agreeing on how much is excessive from a health standpoint and measuring that excess is problematic. Rather than using direct measures of body fat in epidemiology and vital statistics, researchers have relied on simple measurements of weight and height, and the use of these measures to calculate a value known as the **body mass index** (BMI) to trace obesity prevalence. BMI is calculated as weight, expressed in kilograms, divided by the square of height, expressed in meters ( $\text{kg}/\text{m}^2$ ). Thus, BMI offers a measure of weight adjusted for height and this value correlates reasonably well with total body fat in the adult human (2). The assessment of obesity in children will be discussed in detail in Chapter 11 and more information about the measurement of human body composition is available in Chapter 13. Here we caution the reader that the body fat content associated with a given BMI depends critically on the sex, age, race, and developmental stage of the child, presenting difficulties in the use of BMI for assessment of pediatric populations, as will be discussed below.

For cost and other logistical reasons, many epidemiological surveys rely on self-reported (rather than measured) height and weight. This introduces error when BMI is calculated, since respondents often underestimate their weight and overestimate their height (3). Overestimation of height—which is a particular problem because height is squared when BMI is calculated—increases with age and differs by sex, with men overestimating height more than women (3). Underestimation of weight also differs by sex (women underestimate more than men), and by degree of obesity (overweight

persons underestimate weight more than normal-weight persons), and there is also evidence that estimations may differ by ethnicity (4). Such self-reported data can nonetheless provide useful information about trends and regional information that might otherwise be too expensive to obtain. For the purpose of this chapter, we shall rely primarily on data collected through the **National Health and Nutrition Examination Survey** (NHANES), in which both height and weight are measured to yield a more accurate assessment of BMI.

The current classification of overweight and obesity using BMI is shown in Table 1-1. This classification has been adopted by both the National Institutes of Health (NIH) (5) and the Centers for Disease Control and Prevention (CDC) (6) in the US, and by the World Health Organization (WHO) (7). For adults, the BMI categories are age-independent and the same for both sexes. However, a given BMI value may not correspond

**Table 1-1** BMI-associated disease risk

The use of body mass index (BMI) has been proposed by the National Institutes of Health,<sup>a</sup> the Centers for Disease Control and Prevention,<sup>b</sup> and the World Health Organization<sup>c</sup> as a method for defining overweight and obesity. This classification system is based on epidemiologic data indicating that the risk of morbidity and premature mortality usually begins to increase at a BMI of 25–29.9  $\text{kg}/\text{m}^2$ , and increases further at a BMI of 30  $\text{kg}/\text{m}^2$ . Other factors, such as waist circumference, weight gain since young adulthood, fitness level, and ethnic or racial background, also influence the relationship between BMI and overall disease risk

Classification	BMI ( $\text{kg}/\text{m}^2$ )	Risk
Underweight	<18.5	Increased
Normal	18.5–24.9	Normal
Overweight	25.0–29.9	Increased
Obese Class I	30.0–34.9	High
Obese Class II	35.0–39.9	Very high
Obese Class III	$\geq 40$	Extremely high

<sup>a</sup>National Institutes of Health and National Heart, Lung, and Blood Institute. Clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults—the evidence report. *Obes Res* 1998; 6 (Suppl 2): 1S-209S.

<sup>b</sup>Centers for Disease Control and Prevention. Overweight and Obesity: Defining Overweight and Obesity. [www.cdc.gov/nccdphp/dnpa/obesity/defining.htm](http://www.cdc.gov/nccdphp/dnpa/obesity/defining.htm) (accessed June 28, 2008).

<sup>c</sup>World Health Organization. Obesity: Preventing and Managing the Global Epidemic. Report of a WHO Consultation on Obesity. Geneva: World Health Organization, Technical Report Series 2000; 894: 1–253.

**Table 1-2** Waist Circumference and/or Waist-to-Hip Ratio (WHR) Associated with Increased Risk

Men: Waist circumference >102 cm (>40 inches) or WHR $\geq$ 1.0
Women: Waist circumference >88 cm (>35 inches) or WHR $\geq$ 0.8

to the same degree of fatness in all cases. For example, for two individuals with the same BMI, one male and one female, the female will have a greater fat content. Furthermore, a given BMI does not necessarily indicate the same level of disease risk in different ethnic populations (3). This is due, in part, to differing genetic susceptibility and variant fat distribution among ethnic groups.

An increase in central adiposity—the accumulation of body fat in the abdominal area—is associated with greater risk for diabetes and cardiovascular disease (8–9) and also for cancers of the colorectum, pancreas, breast, and **endometrium** (10). To monitor the distribution of fat in the body for the purpose of assessing this risk, the circumference of the waist is measured. Waist circumference is unrelated to height (11) but correlates well with BMI (12) and total body fat (13). In some studies, the ratio of the circumference of the waist to the circumference of the hips (commonly referred to as the waist-to-hip ratio or WHR) is used for this purpose. Table 1-2 shows the thresholds for waist size and WHR suggested by both NIH (5) and WHO (7) for determining increased health risk associated with central adiposity.

Classifying obesity in children is more difficult for a number of reasons. Because children are growing, normal values of BMI differ as the child ages and matures. Although the pattern differs somewhat by sex, BMI values rise steeply during infancy, decline during the pre-school years, and then rise again in childhood and adolescence until the child reaches adulthood. For this reason, BMI growth charts represent the distribution of normal BMI values for children of a specific age and sex. To use the BMI growth chart, one must know the child's age (to the closest month) in addition to height and weight *at that age*.

In the past, the most widely used growth reference was developed by the US National Center for Health Statistics (NCHS) of the Centers for Disease Control and Prevention (CDC), which used tables of weight-for-height in children aged 2 years and more, and weight-for-length in children from birth to 2 years (in infants, recumbent length is measured in lieu of standing height). In 2000, the CDC published new BMI-for-age tables based on data from five nationally representative surveys conducted in the US from 1963 to 1994, with the excep-

tion that all weight data from children ages 6 and older in 1988–94 were excluded because of increases in body weight observed over that period (3). These sex-specific **BMI growth charts** are used for children aged 2–20 years (see Figures 1-1 and 1-2) and replace the 1977 NCHS weight-for-height charts.

#### Box 1-1 Definitions of childhood overweight, obesity, extreme obesity

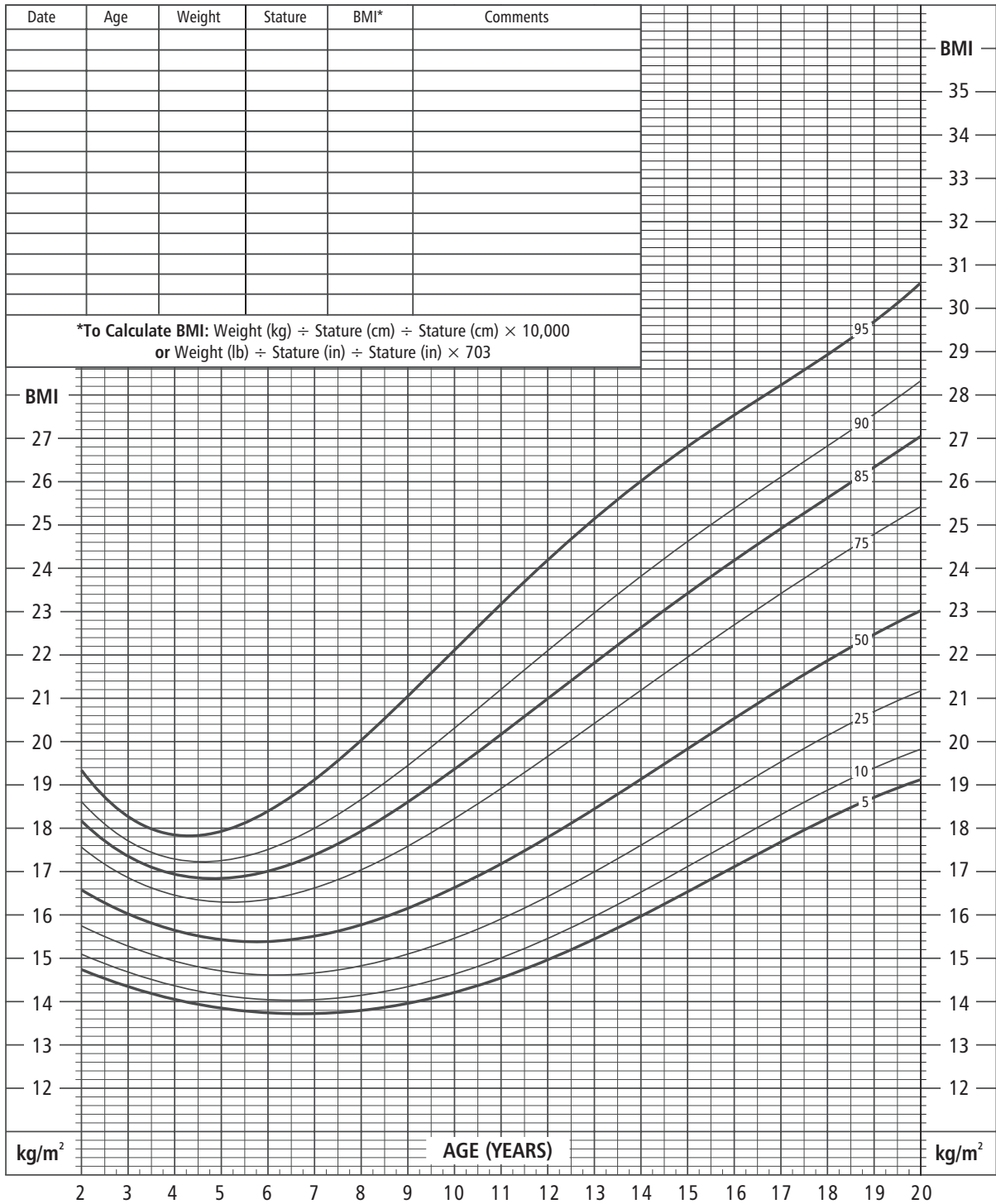
BMI-for-age is used to identify children and adolescents at the upper end of the distribution. Those who are “obese” have a sex- and age-specific BMI that is  $\geq$ 95th percentile. Prior to 2005, these children were referred to as “overweight”; the term “obese” was not used. The sex- and age-specific BMI  $\geq$  85th and  $<$ 95th percentile refers now to children who are “overweight” but previously those children were designated as “at risk for overweight” (14–15). The **Institute of Medicine** (IOM) convened a group of experts who recommended that this terminology be changed to categorize children at or above the 95th percentile as “obese” and children between the 85th and 95th percentiles as “overweight” (16) and in 2007 experts convened by the American Medical Association and other groups recommended that this new terminology be widely accepted and used for the assessment and treatment of children (17). Extreme obesity in children has been identified as  $\geq$ 99th percentile (18) although it has been pointed out that the highest percentile available on the CDC 2000 growth charts is the 97th percentile (19). An alternative definition that may be better accepted is to consider any child  $\geq$ 120% of the 95th percentile of BMI as extremely obese (20). One study of more than 710,000 children in southern California found that 6.4% met the latter definition of extreme obesity (21). It has been pointed out that if this prevalence holds for US children nationally, extreme pediatric obesity prevalence exceeds that of extreme adult obesity prevalence (22), which is currently estimated at 5.7% (23).

In 2006, the WHO published a set of growth charts that were based on measurements of healthy, breastfed children from around the world (24). The WHO charts are intended to offer a standard of physiologic growth and not a descriptive reference (3). In many studies of children, “overweight” and/or “obesity” are often defined using standard deviation (SD) scores, or z-scores, which the reader may encounter. In this system, a child with a BMI z-score of +2 is 2 standard deviations above the mean BMI for the reference population in which BMI values are normally distributed (25). BMI z-scores are useful in a school or community setting to evaluate

**2 to 20 years: Boys**  
**Body mass index-for-age percentiles**

NAME \_\_\_\_\_

RECORD # \_\_\_\_\_



Published May 30, 2000 (modified 10/16/00).  
 SOURCE: Developed by the National Center for Health Statistics in collaboration with  
 the National Center for Chronic Disease Prevention and Health Promotion (2000).  
<http://www.cdc.gov/growthcharts>

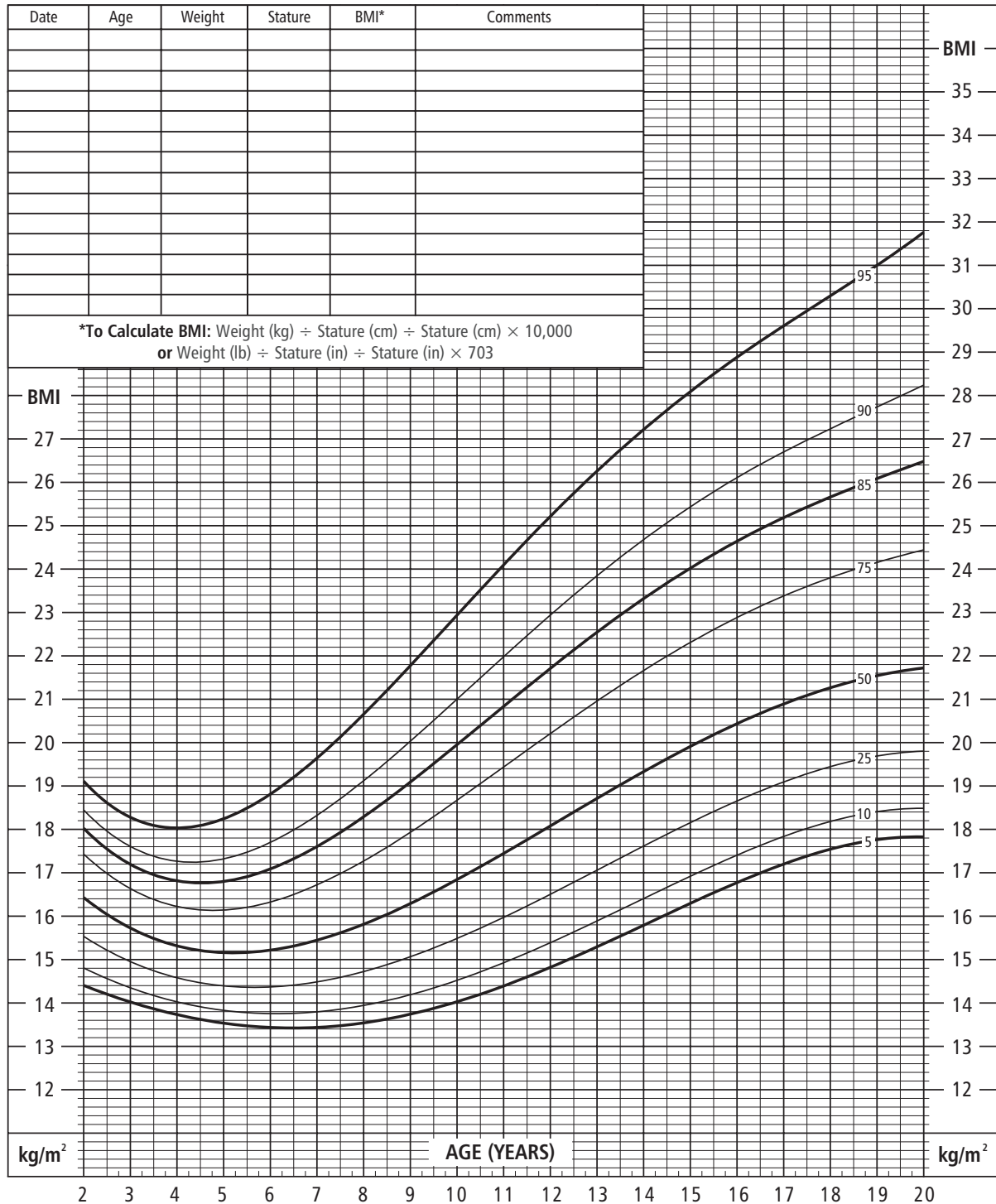


**Figure 1-1** CDC growth chart—BMI for age percentiles for boys (2–20 years old)

2 to 20 years: Girls  
Body mass index-for-age percentiles

NAME \_\_\_\_\_

RECORD # \_\_\_\_\_



Published May 30, 2000 (modified 10/16/00).  
SOURCE: Developed by the National Center for Health Statistics in collaboration with  
the National Center for Chronic Disease Prevention and Health Promotion (2000).  
<http://www.cdc.gov/growthcharts>



Figure 1-2 CDC growth chart—BMI for age percentiles for girls (2–20 years old)

progress when programs are implemented to prevent the development of childhood obesity.

The CDC growth charts and the WHO standards are intended for clinical use in monitoring the growth of children over time. An historical perspective on the growth pattern of a child through repeated (e.g., yearly or six-monthly) measurements and plotting of BMI on a growth chart can be used to identify a growth trajectory that is heading toward overweight or underweight (failure to thrive). The use of either percentiles or z-scores to categorize a child as overweight or obese is a secondary purpose (26) that can be useful from an epidemiological standpoint, when the goal is to estimate prevalence. These scores can also be useful to screen groups of children to identify those who might be obese and refer them for a more in-depth assessment by a qualified health professional. An analysis of 1999–2004 NHANES (see below) data by Flegal and colleagues in more than 8,800 8–19 year olds (51% boys) showed that most children at or above the 95th percentile indeed have a high adiposity as measured using DXA scans (27). This study showed that results varied by race or ethnicity, especially in the overweight category (85th–95th percentile). Since there are no widely accepted levels of body fatness that define high adiposity for children, the development of body fat standards in children is an important research need. Flegal (27) illustrate the need to take race or ethnicity into account in the development of such standards.

Currently, there are no agreed definitions of obesity or body fat standards among infants and children younger than 2 years old. For this age group, weight-for-length percentiles from the 2000 CDC growth charts are used to evaluate growth. To qualify a child for enrollment in the Special Supplemental Nutrition Program for Women, Infants, and Children (WIC), the 95th percentile on the 2000 CDC sex-specific BMI charts is sometimes used to establish program eligibility for children age 2 or older. Excessively rapid growth in children 0–2 years of age cannot be used as an eligibility criterion to qualify a child for enrollment in WIC, despite concerns that this is a “critical period” of development, and rapid weight gain during this time may predispose a child to lifelong obesity (28). A pressing research need is to clearly define infant obesity, elucidate predisposing factors, and develop effective interventions (see Chapter 25 and 27). Preliminary research suggests that the prevalence of obesity in infants may be as high as 16% and is a predictor of obesity at 2 years of age (29) when growth can be assessed using the BMI growth charts.

### Surveying obesity prevalence

It is usually impractical to gather data from medical records or vital statistics to estimate the prevalence of

obesity. Surveys or studies of large populations are useful for this purpose.

### United States National Center for Health Statistics

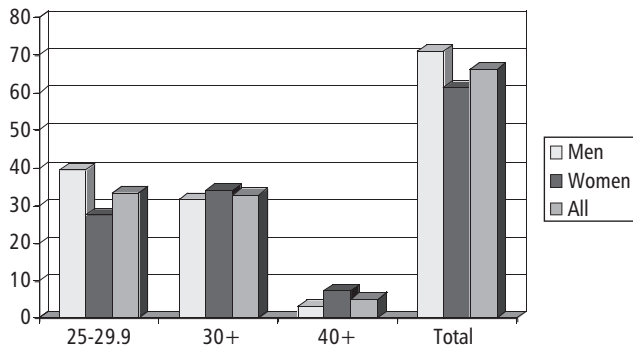
National-level data for the US (i.e., data that are representative of the nation taken as a whole) are gathered by the National Center for Health Statistics (NCHS) of the Centers for Disease Control and Prevention (CDC) from measured data obtained through NHANES (30). NHANES is designed to monitor the health and nutritional status of the civilian, non-institutionalized population, aged 2 years and older. NHANES (31) includes standardized health examinations in a mobile examination center on a representative cross-sectional sample of the US population.

Originally conducted every decade or so since it was founded in the early 1960s, starting in 1999, NHANES has been conducted on a continuous basis, surveying approximately 5,000 people each year (32). NHANES is the primary source for national data on overweight and obesity in adults, adolescents, and children. Because of the expense involved, NCHS also collects self-reported data obtained by telephone through the Behavioral Risk Factor Surveillance System (BRFSS) (33). Although they underestimate prevalence, these data are useful for determining state-by-state prevalence and changes in prevalence in a state over time. Because it is more reliable, wherever possible we will be discussing primarily NHANES data based on measured height and weight.

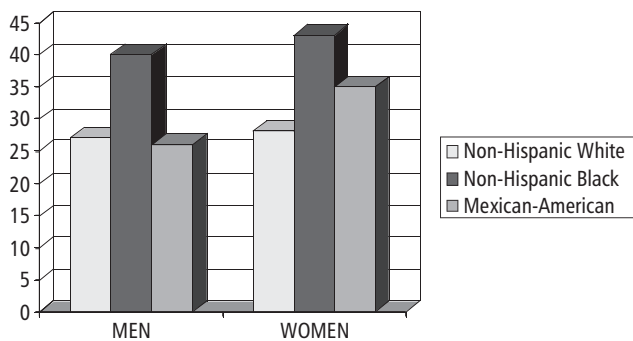
### Prevalence in adults

In adults, a BMI of 30 or higher is a widely accepted definition of obesity and has been used in the US for decades. A BMI of 30 corresponds roughly to 13.5 kg of excess weight. Data from NHANES 2007–8 show that the prevalence of obesity is 34% among adults—approximately 80 million people (34). Whereas the increase in obesity has occurred in all subgroups in recent decades, obesity is more common in women (35.5%) than in men (32.2%) (34). As shown in Figure 1-3, the prevalence of extreme obesity (BMI  $\geq$  40) in 2003–4 was 2.8% in men and 6.9% in women (35). Interestingly, the rate of increase has slowed such that there was no significant increase in the prevalence of obesity between NHANES 1999–2006 and NHANES 2007–8 for adult men or women (34). However, the prevalence of severe obesity (approximately 45.35 kg excess weight) continues to escalate (36).

In 2005–6, African Americans, Mexican Americans, persons with low income, adolescents (12–19 years), and adults 60 years or older were over-sampled in NHANES. Large disparities in obesity prevalence in different ethnic



**Figure 1-3** Percent overweight, obese, extremely obese, by BMI (U.S. adults ages 20–74, NHANES 2003–2004)



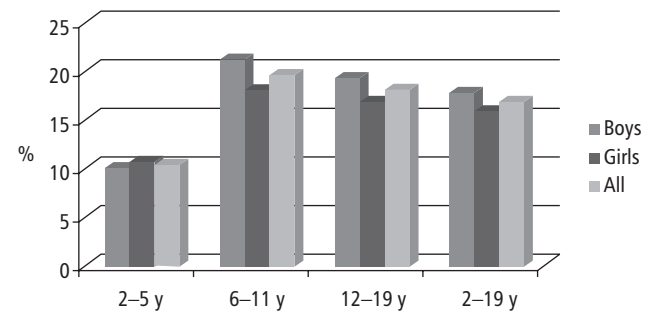
**Figure 1-4** Percent obese among 20- to 39-year-old adults, by ethnicity (U.S. adults, NHANES 2005–2006)

groups were documented among adult women, with the highest prevalence among Blacks and Mexican Americans as compared to Whites (34). For women aged 40–59 years, obesity prevalence is 53% among non-Hispanic Blacks, 51% among Mexican Americans, and 39% among Whites (34). For adults of childbearing age (20–39 years), the differences among the various ethnic groups are shown in Figure 1-4. These data are of particular concern given the growing number of studies showing an association between parental, especially maternal, obesity and the development of obesity in the offspring (37). This association will be discussed further in Chapter 10.

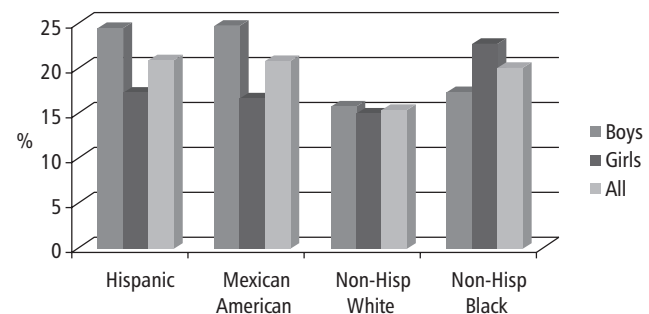
### Prevalence in children and adolescents

Through NHANES, the National Center for Health Statistics (38) has systematically collected data on obesity in children and adolescents since 1963 (see Figure 1-5).

The rate of increase in obesity prevalence among US children has escalated sharply since the 1970s, prompting the Congress in 2002 to mandate that certain federal



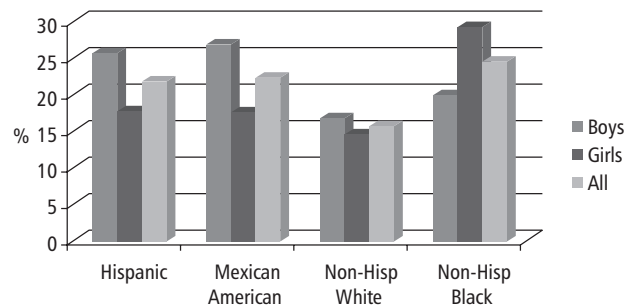
**Figure 1-5** Percent obese among children 2–19 years (U.S. NHANES 2007–2008)



**Figure 1-6** Percent obese among children 2–19 years, by ethnicity (U.S. NHANES 2007–2008)

agencies fund the Institute of Medicine (IOM) to develop an action plan to prevent childhood obesity (39). The resulting report was published in 2005 and highlighted the rapid increase in childhood obesity prevalence, the medical urgency of the problem, and the usefulness of NHANES data in documenting important details of the epidemic, such as the disparities in obesity prevalence among non-Hispanic Whites, non-Hispanic Blacks, and Mexican Americans (39). Based on NHANES data for the period 2003–4, the prevalence of obesity for US children aged 2–19 is 17.1% (3). Figure 1-6 summarizes NHANES data for the period 2007–2008 and demonstrates that prevalence differs by ethnicity: for all White children it remains at 15%, but for all Black children it is 20% and for all Mexican American and Hispanic children it is 21% (23).

There is evidence that for obese adolescents the chance of progressing to obesity in young adulthood ranges from 70% to 80% (37). Thus, the high prevalence rates among adolescents (shown in Figure 1-7), especially among non-Hispanic Blacks and Mexican Americans, is of particular concern (23).



**Figure 1-7** Percent obese, adolescents 12–19 years, by ethnicity (U.S. NHANES 2007–2008)

The CDC has identified the development of innovative childhood obesity practices as an important priority (40) since there are now more than 12 million obese children in the US, with several million of those severely obese (41). Childhood obesity treatment and prevention are discussed further in Chapters 25 and 26–27, respectively.

### BRFSS and YRBS

To ensure that NHANES is nationally representative, it is not necessary for the mobile examination centers to enter all states in the US; consequently, NHANES is not useful for collecting state data. To address this gap in the data, as mentioned earlier, the Behavioral Risk Factor Surveillance System (BRFSS; see [www.cdc.gov/brfss](http://www.cdc.gov/brfss)), an ongoing, state-based, random-digit-dialed telephone survey of the non-institutionalized civilian population aged > 18 years, is used. BRFSS data allow the assessment of the prevalence of obesity among adults categorized by state and **demographic characteristics**, and are particularly useful in guiding policy and program development at the state and local level. Among youth, an analogous telephone survey system, the Youth Risk Behavior Survey (YRBS; see [www.cdc.gov/HealthyYouth/yrbs/index.htm](http://www.cdc.gov/HealthyYouth/yrbs/index.htm)), permits the collection of data on health-related behaviors, as well as on self-reported height and weight.

### Global prevalence

Although few countries have nutrition and health monitoring systems equivalent to NHANES or BRFSS for assessing obesity prevalence, it is clear that the increase in obesity is occurring not only in the US, but throughout the world. The WHO has declared obesity as one of the world's top 10 risk conditions and one of the top five in developed nations (42). There are areas of the world, such as the South Pacific island countries of Tonga and Nauru, where there has been such an enormous increase in obesity that the majority of the adult population is

now obese according to the WHO (43–44; see also Table 1-3). This is true also of some sub-populations in the developed world, such as the Pima Indians in Arizona, where 70% of the population is obese (45). WHO data from Latin America and even Africa show a growth of obesity in these regions as well (44; and see Table 1-3).

WHO global estimations of prevalence indicate that approximately 1.6 billion adults (aged 15+) were overweight and at least 400 million were obese in 2005 (46). In addition, at least 20 million children under the age of 5 years were obese as of 2005 (46). An estimated 12.5 million children in the US are obese (40), with 2.8 million of those children categorized as severely obese (41). The WHO further projects that by 2015 approximately 2.3 billion adults will be overweight and more than 700 million will be obese (46). Table 1-3 lists overweight and obesity prevalence figures for adults in 66 countries. The WHO obesity prevalence data shown in this table for China (3.0%), the world's most populous country, are likely to be low since a 2008 estimate of obesity prevalence based on BMI reported that 22.8% of Chinese adults are overweight and 7.1% are obese (47). The epidemic of overweight or obesity is affecting children and even infants (48). Indeed, a 2007–8 national estimate of type 2 diabetes prevalence in China found that nearly 10% of the adult population (92.4 million people) are frankly diabetic and another 16% (148.2 million people) have pre-diabetes (48).

Evidence from the Caribbean (Barbados, Cuba, Jamaica, and Saint Lucia) indicates that obesity is a growing problem in this region (7). The growth in obesity prevalence is accompanied by a higher prevalence of diabetes, cardiovascular disease, and hypertension (7). Experience in Cuba over the past two decades is illustrative of the profound impact of obesity on health. In contrast to many developing countries, Cuba has an extensive healthcare system and a well-developed system for tracking vital events (49). Consequently, it is known with certainty, for example, that life expectancy in Cuba is 77 years and cardiovascular disease is the leading cause of death (49–50).

Since the 1960s, Cuba has been subjected to an economic embargo by the US. In 1989, after losing the Soviet Union as an important trading partner, Cuba entered a prolonged crisis, which is referred to as the “Special Period” (49–50). The crisis deepened from 1989 to 1995 with economic output in 1995 only half the level in 1990. Foreign trade contracted by 80%, with reduced imports, limited fuel availability, and a scarcity of many food items. Food was rationed and 40% reductions in per capita daily energy intake were documented (50) along with significant increases in walking and cycling as public transportation became unavailable (49).



**Table 1-3** National Overweight and Obesity Prevalence Rates in Adults in 66 Countries

Country	Year of Survey	Measured/ Self-reported	Age Range	% Overweight (BMI $\geq$ 25)			% Obese (BMI $>$ 30)		
				Male	Female	Both Sexes	Male	Female	Both Sexes
Australia	1995	Measured	19+	64.3	47.3	55.3	18.7	18.4	18.6
Austria	1991	Unknown	20+	—	—	—	8.3	9.0	8.5
Bahrain	1998–99	Measured	19+	59.9	62.4	61.2	23.3	34.1	28.9
Belgium	1979–84	Measured	25–74	58.6	53.6	56.2	12.1	18.4	15.1
Brazil	1989	Measured	25–64	27.3	38.1	32.8	4.8	11.7	8.3
Canada	2000–1	Self-reported	20–64	55.6	39.2	47.4	16.0	13.9	14.9
China	1990–2000	Measured	20+	22.4	26.3	24.5	2.0	3.9	3.0
Cook Islands	1998	Unknown	17+	76.6	81.0	77.6	40.6	50.0	43.0
Croatia	1995–97	Measured	18–65	79.2	49.9	64.4	31.1	15.2	23.1
Cuba	1982	Measured	20–59	31.5	39.4	36.4	—	—	—
Cyprus	1993–94	Measured	Adults	—	—	—	16.0	19.0	—
Czech Republic	2002	Self-reported	16+	56.7	47.4	51.7	13.7	16.3	15.1
Denmark	1994	Self-reported	16+	44.2	28.0	35.8	8.2	7.0	7.6
Egypt	1998–99	Measured	18–60	48.9	71.1	62.1	12.6	33.0	24.7
Estonia	1997	Measured	19–64	41.9	29.9	35.4	9.9	6.0	7.8
Fiji	1993	Measured	18+	32.4	50.4	41.7	7.3	20.5	14.1
Finland	1999	Measured	15–64	50.1	36.0	42.4	9.7	10.5	10.1
France	1991–92	Self-reported	20+	40.8	28.9	35.0	6.4	7.8	6.9
French Polynesia	1995	Unknown	16+	75.2	72.5	73.7	36.3	44.3	40.9
Gambia	1995	Measured	15+	—	—	10.4	—	—	2.3
Germany	1998	Measured	18–79	66.7	53.8	60.0	19.2	22.3	20.8
Ghana	1987–89	Measured	20–65	5.3	18.1	11.2	0.6	6.1	3.1
Greece	1997	Measured	30–82	—	—	—	—	—	—
Hungary	1992–94	Measured	18+	62.9	49.1	55.4	21.0	21.2	21.1
India	1998	Measured	18+	4.3	4.5	4.4	0.3	0.5	0.5
Iran	1999	Measured	15+	29.3	38.6	34.4	5.6	14.2	10.3
Ireland	1997–99	Measured	18–64	66.4	48.4	56.8	20.1	15.9	17.8
Italy	1994	Self-reported	15+	46.0	31.4	38.4	6.5	6.3	6.4
Japan	2001	Measured	15+	26.8	20.7	23.4	2.9	3.3	3.1
Kuwait	1998–2000	Measured	18+	65.8	62.6	64.2	27.5	29.8	28.8
Kyrgyzstan	1993	Measured		31.5	38.1	35.0	4.8	12.1	8.7
Lao People's Democratic Republic	1994	Measured	18+	6.8	11.4	9.3	0.7	1.4	1.1
Latvia	1997	Measured	19–64	50.5	50.4	50.4	9.5	17.4	13.7
Lesotho*	1993	Measured	20–65	—	50.1	—	—	23.0	—
Lithuania	1997	Measured	19–65	53.5	51.0	52.0	11.4	18.3	15.1
Malaysia	1996	Measured	20+	24.1	29.0	26.5	4.0	7.6	5.8
Mauritius	1998	Measured	20+	41.0	54.0	48.1	8.0	20.0	14.4
Mexico	1999	Measured	18–49	—	59.6	—	—	24.4	—
Morocco	1988–99	Measured	18+	25.4	45.0	35.5	4.3	16.0	10.3
Nauru	1994	Measured	25–69	—	—	—	80.2	78.6	79.4

(Continued)

Table 1-3 (Continued)

Country	Year of Survey	Measured/ Self-reported	Age Range	% Overweight (BMI ≥ 25)			% Obese (BMI > 30)		
				Male	Female	Both Sexes	Male	Female	Both Sexes
New Caledonia*	1992–94	Measured	30–59	—	70.4	—	—	—	—
New Zealand	1996–97	Measured	15+	41.0	29.8	34.6	12.6	16.7	14.9
Norway	1994	Self-reported	16–79	42.0	26.4	34.0	5.0	5.9	5.4
Pakistan	1990–94	Measured	15+	10.5	17.5	13.8	1.6	5.7	3.4
Peru	2000	Measured	18–75	52.0	58.0	55.4	11.5	19.9	16.3
Philippines	1998	Measured	20+	17.0	23.3	20.2	2.1	4.4	3.3
Republic of Korea	1998	Measured	19+	26.0	26.5	26.3	1.7	3.0	2.4
Russia	1996	Measured	18+	44.2	58.4	—	10.8	27.9	—
Saudia Arabia	1995	Measured	18+	40.3	45.5	43.3	13.1	20.3	17.2
Serbia & Montenegro	2000	Measured	20+	—	—	54.0	—	—	17.6
Seychelles	1994	Measured	25–64	38.3	59.8	49.7	8.5	28.2	18.9
Singapore	1998	Measured	18–69	33.9	27.0	30.4	5.3	6.7	6.0
South Africa	1998	Measured	15+	29.2	56.3	45.1	9.4	30.1	21.6
Spain	1995–97	Self-reported	25–64	—	—	—	12.3	12.1	12.2
Sweden	1996–97	Self-reported	16–84	45.9	33.6	39.6	6.8	7.2	7.0
Switzerland	1992–93	Self-reported	15+	39.2	21.8	30.3	6.1	4.7	5.4
Thailand	1996	Measured	13–59	13.2	25.0	—	—	—	—
The Netherlands	1996–98	Measured	20+	43.5	36.5	—	6.5	9.1	—
Tonga	1998–2000	Measured	15–70	—	—	—	—	—	56.0
Tunisia	1996–91	Measured	20–59	29.7	50.9	43.8	6.4	22.7	17.2
Turkey	1997	Measured	20+	—	—	—	12.9	29.9	22.3
United Kingdom	1986–87	Measured	16–64	45.0	36.0	40.5	8.0	12.0	10.0
United States	1999–2002	Measured	16+	65.6	59.5	—	25.8	31.8	—
Uruguay	1998	Self-reported	18+	57.0	49.0	52.4	17.0	19.0	18.1
Vanuatu	1998	Measured	20+	45.9	51.9	48.9	12.2	19.6	15.9
Vietnam	1987–89	Measured	15+	—	—	—	—	—	—

\*Female data only.

United Nations System Standing Committee on Nutrition. Overweight and Obesity: a new nutrition emergency? SCN News 29, Late 2004–Early 2005, Table 1: 7–8. [www.unscn.org/layout/modules/resources/files/scnnews29.pdf](http://www.unscn.org/layout/modules/resources/files/scnnews29.pdf) (accessed August 18, 2010).

Complete economic recovery did not occur until 2000, so the Special Period lasted approximately a decade.

In 1993, as a consequence of an outbreak of neuropathy, nutritional studies documented that 27% of Cubans had lost 10% or more of their body weight over the previous 12 months and 43% experienced severe caloric restriction (49). This unfortunate **natural experiment** permitted researchers to measure the effects of this population-wide weight loss on mortality from cardiovascular disease and type 2 diabetes. The prevalence of obesity decreased from 11.9% to a low of 5.4% at the peak of Special Period. Physical activity—walking and

cycling—increased, from 30% considered physically active before the crisis to a high of 70% considered physically active in 1995. This change was apparently sustained at 67%, as documented by national surveys in 2001 (49).

Substantial declines in mortality from **coronary heart disease** (a drop of 35%), type 2 diabetes (down 51%), and all-cause mortality (down 18%) were documented between 1995 and 2002, while rates of cancer mortality, which are not sensitive to obesity (see discussion below), remained relatively constant (49). The BMI distribution for the entire population shifted to the left: mean BMI

decreased from 24.8 in 1991 to 23.3 in 1995, reflecting a 50% reduction in obesity prevalence (49).

It is likely that the Special Period is the first demonstration of sustained negative energy balance—with documented high levels of physical activity and weight loss that lasted 4–8 years—producing significant reductions in diabetes and cardiovascular disease mortality (49). There was a shift in diet composition in Cuba during the Special Period with carbohydrate intake increasing from 65% to 77% of calories as sugar cane and rice became the primary sources of energy (49). As the availability of animal products declined, fat intake decreased from 20% to 13% of calories and protein intake fell from 15% to 10% of calories—a diet composition considered diabetogenic by some authorities, yet accompanied by marked decreases in diabetes mortality (49).

There were many negative consequences of the Special Period: tuberculosis deaths increased by 48% (49); more elderly persons died, primarily of infections; the decline in infant mortality was interrupted for three years, and the incidence of low birth weight increased from 7.3% to 9.0% (49). An epidemic of optical and peripheral neuropathy attributed to vitamin and protein deficiencies affecting at least 50,000 people, was documented between 1992 and 1993 (49).

When the Special Period ended, the Cuban economy started to grow, productivity increased, energy and food availability increased, and public transportation improved. The nadir in mortality from type 2 diabetes and heart disease was reached in 2001 and mortality from these causes increased for the next four years. Like most countries, Cuba now faces the challenge to craft public health initiatives to stem this increase. The Special Period suggests the potential public health impact that could be achieved with a population intervention designed to maintain nutritional sufficiency while boosting physical activity and moderating calorie intake. With a current life expectancy of 78.6 years, Cuba's health system, including its Rural Social Medical Service, emphasizes disease prevention (high vaccination rates and high proportion of births attended by skilled health workers) and primary healthcare (65% of physicians practice primary care medicine), achieving “developed-world health outcomes with a developing-world budget” (50). In contrast to the US, Cuba has been forced to rely more on education (community health literacy) than on medical supplies and sophisticated technologies to maintain a healthy population at a per capita cost of \$355 (7.1% of total Gross Domestic Product) as compared to \$6714 (15.3% of total GDP) in the US (50). As the economy stabilizes and obesity prevalence increases in Cuba, it will be interesting to see what strategies are used to stem the problem.

## Consequences of obesity and overweight

The consequences of obesity cover a wide spectrum of social, medical, and economic domains (7). Obesity is associated with diminished health and psychosocial well-being, reduced socioeconomic prospects of affected individuals and populations, and lower economic productivity of the workforce. Obesity is a major contributor to the higher healthcare costs of businesses and insurance providers, as well as workers. It contributes to decreased longevity and increased disability, as well as increased reliance on surgical procedures and medical interventions to treat obesity or to manage the various comorbidities of obesity (7).

### Health

There are dozens of health conditions that are associated with obesity either directly or indirectly (see Chapter 12). In the following sections, we discuss a selected few disease conditions that are highly prevalent and whose prevalence is increasing as a consequence of the growing epidemic of obesity.

#### Type 2 diabetes

Among adults, the relationship between BMI and type 2 diabetes is perhaps stronger than it is for any other obesity comorbidity (3). It has been estimated that 64% of male and 77% of female cases of type 2 diabetes could be prevented if no one had a BMI above 24; or the reductions would be 44% and 33%, respectively, if no one had a BMI above 29 (51–52). The American Diabetes Association (53) estimates that about 19 million people in the US have type 2 diabetes, and another 54 million are “pre-diabetic,” which means that increasing weight gain in this latter population places them at extremely high risk for the development of frank diabetes. The mortality associated with diabetes is 73,000 people a year in the US, which makes it the fifth leading cause of death (53).

The Diabetes Prevention Program (DPP) targeted overweight pre-diabetic individuals and demonstrated that lifestyle change—weight loss, increased physical activity, and the adoption of a low-fat diet—outperformed a leading diabetes drug in preventing conversion from pre-diabetes to frank diabetes (54). The DPP was a remarkable demonstration of the value of lifestyle change in the prevention of diabetes in high-risk overweight individuals. Lifestyle change was protective against conversion to diabetes in 58% of the cases, whereas the drug prevented only one third of the cases (54). Similar findings from a Finnish study of individuals with impaired glucose tolerance were reported in 2001 (55). It is worth noting that data from the Diabetes

Prevention Program Research Group demonstrate that of the lifestyle changes accomplished by the participants in the DPP, weight loss had the greatest effect in preventing diabetes (56).

Once diabetes is established, it is notoriously difficult to treat with lifestyle change, and adjunctive medical treatment is usually required. Observational studies have shown that **bariatric surgery** can be useful in bringing about complete remission of diabetes (57). A recent study examined the use of surgery in diabetic obese individuals with a BMI between 30 and 40 (58). This non-blinded, randomized controlled trial of weight loss induced by bariatric surgery vs. weight loss through lifestyle change was conducted in newly diagnosed diabetic patients. The results demonstrated significant weight loss (20.7% of initial body weight) with bariatric surgery and remission of the disease in 22 out of 30 patients (73%), which compared to remission in only 4 out of 30 patients (13%) in the lifestyle change group (58). The average weight loss in the lifestyle change group was only 1.7% of initial body weight, considerably less than that achieved in the DPP. This disappointing result may have been a consequence of inadequate programmatic support or the refractoriness to weight loss in patients once frank diabetes is established (58). Nonetheless, this study demonstrates the interesting and puzzling relationship between diabetes and obesity, which is the focus of intensive research efforts. The use of bariatric surgery for the treatment of obesity will be discussed in greater detail in Chapter 19.

In the pediatric population, type 2 diabetes is a very low prevalence condition (3), but is an emerging concern because it is rapidly increasing (59), especially in communities with a large population of ethnic minorities such as African American children, Native American children, children of Asian/South Pacific Islanders, or children of Hispanic origin. It is also an issue of increasing concern in sparsely populated rural communities, such as those in the majority of counties in Montana, where the population tends to be White and poor (see Chapter 27).

Among adolescents, preliminary reports identify alarmingly high rates of type 2 diabetes in the ethnic populations identified above, with the vast majority (> 90%) of those individuals classified as overweight (60). Data from NHANES showed a prevalence of diabetes (types 1 and 2 combined) of 9.3% in the adult population, with an additional 26% having impaired fasting glucose (5.6– < 7.0 mmol/L) (61). As will be discussed below, the cost associated with the treatment of type 2 diabetes is the major determinant of the direct economic costs of obesity.

### Cardiovascular disease, hypertension, and stroke

Cardiovascular disease (CVD) includes coronary heart disease (CHD) and peripheral vascular disease. The evidence is strong that obesity is a major independent risk factor for CVD for men (62) and women (63), and that weight reduction leads to an improvement in various cardiovascular parameters. In addition to obesity and CVD linkages through hypertension, dyslipidemia (especially low levels of high-density lipoproteins and high levels of circulating triglycerides), insulin resistance, and impaired glucose tolerance (64), the role of inflammation as an important risk factor is an emerging focus of active research (65). The greater the degree of obesity, the higher the risk of CVD (66). There are ethnic groups, such as Asian Indians, with high rates of CHD associated with a constellation of risk factors that differs somewhat from that occurring in White groups (67). Nevertheless, the relative increase in risk associated with increasing degrees of obesity is fairly similar throughout the world (7).

Elevated intra-abdominal (central) fat accumulation appears to play a key role in raising risk for heart disease, especially in men. The WHO has summarized characteristics of intra-abdominal fat that have been postulated to play a role in raising CHD risk (7), possibly by promoting insulin resistance. They are:

- Increased fat cell number.
- Higher rate of blood flow per unit tissue mass.
- Elevated glucocorticoid (cortisol) receptor number.
- Elevated **androgen receptor** number.
- Increased **catecholamine**- (epinephrine and norepinephrine) induced lipolysis (the breakdown of stored fat to release free fatty acids and glycerol).

The increased receptor number in abdominal fat may make it more susceptible, for example, to stress-induced hormonal stimulation. Since abdominal fat cells are located “upstream” from the liver, delivering fatty acids to the liver by way of the portal circulation, a high-stress lifestyle may expose the liver to high levels of nonesterified fatty acids in an individual with abdominal obesity—a scenario in which insulin resistance, dyslipidemia, and the full-blown **metabolic syndrome** (see below) may be more likely to develop (7). The specific linkage between abdominal obesity and disease consequences, especially the metabolic syndrome, is another area of intensive research.

Both systolic and diastolic blood pressure increase with increasing BMI (68–70) and higher rates of hypertension—defined in these studies as a systolic

blood pressure of  $\geq 140$  mmHg, a diastolic blood pressure of  $\geq 90$  mmHg, or both—among obese persons as compared to lean are the consequence (68). An increased risk for hypertension has been shown for BMI  $\geq 23$  and blood pressure tends to improve with weight loss (70).

The connection between obesity and stroke has received less research attention, but a longer duration of obesity raises the risk of both hypertension and stroke (7, 71). The mechanism of these effects is unclear, but it is thought that the higher circulating levels of insulin associated with insulin resistance in obese persons may cause increased renal retention of sodium, with a resulting increase in blood pressure (7, 72), raising the risk of stroke.

### Gall bladder disease

An increased risk of gallstone formation and gall bladder disease has been shown at a BMI  $\geq 25$  (73) and gallstones are more common among obese persons as compared with their lean counterparts (74–75). It is important to note that the risk of gallstone formation increases with weight loss, especially precipitous weight loss (73). Since the weight loss following bariatric surgery can be rapid, it is not unusual for persons undergoing a bariatric procedure to undergo simultaneous cholecystectomy (removal of the gall bladder).

Congenitally obese mice and lean mice fed a high-fat diet have increased gallbladder wall lipids and poor gallbladder emptying (76). Al-Azzawi and colleagues tested the hypothesis that compared to patients with a normal gallbladder, patients with inflammation of the gallbladder (with or without the presence of gallstones) would have increased gallbladder wall fat. Sixteen patients who underwent gallbladder removal for **cholecystitis** (without gallstones), 16 non-diseased controls who underwent incidental cholecystectomy during surgery for liver or pancreatic disease, and 16 diseased controls whose gallbladder was removed for chronic gallstone formation were studied. Pathology specimens were reviewed in a blinded fashion for gallbladder wall fat, wall thickness, and inflammation. The results were consistent with the hypothesis that increased infiltration of the wall of the gallbladder by fat may lead to poor gallbladder emptying and the development of biliary symptoms (76).

It has been suggested that the propensity for gallbladder disease may be inherited. But Katsika and colleagues (77) examined a large Swedish twin registry and found a doubling of risk for gallstone formation in overweight persons and a more than tripling of risk among obese persons, but no differences between **dizygotic** or discordant **monozygotic** twins (77). Taken together, these findings suggest an important role for environmental

factors in the development of gallbladder disease associated with obesity.

### Osteoarthritis

Osteoarthritis of the knee, hip, and back is strongly associated with obesity (78–80). An increased risk of osteoarthritis has been shown at BMI  $\geq 25$  (80), in studies in which confirmation of the condition was made with radiographic evaluation. Osteoarthritis becomes a comorbidity of obesity when lifestyle is affected, especially when physical activity is curtailed or treatments are required. Weight loss decreases symptoms of osteoarthritis and improves the management of the condition in weight-bearing joints (80–81).

### Sleep apnea/obesity hypoventilation syndrome

Obesity is the single most important cause of **sleep apnea/obesity hypoventilation syndrome**, which is characterized by brief periods during sleep when breathing ceases and, in some cases, hypoxemia occurs. A strong predictor of this condition is upper body obesity, especially in males (78, 82). Confirmation of the condition is made by a formal sleep study. Sleep apnea contributes to impaired alertness during the day, which may contribute to reduced productivity on the job. It is a serious condition that interferes with the quantity and quality of sleep, and is a risk factor for premature death (78, 82–83). Weight reduction can be very effective in controlling sleep apnea (84–85).

### Cancer

A 2007 report, promulgated jointly by the World Cancer Research Fund and the American Institute for Cancer Research (10), presents evidence that elevated body fat is linked to increased risk of cancer in the esophagus, pancreas, gallbladder, liver, colorectum, breast (in postmenopausal women), endometrium, and kidney (10). Table 1-4 summarizes the conclusions of this report regarding the quality of the evidence linking elevated body fatness to the increased risk of these cancers. Note that the evidence of highest quality is identified in the table as “convincing” and the evidence achieves this standard for six of the eight cancers identified above. Note also that for certain cancer sites the notation “Abd” denotes abdominal obesity, which refers to increased fatness in the upper body, usually indicated by a waist circumference of 101.5 cm or more in males and 89 cm or more in females (10). However, with respect to cancer mortality, one study estimates that only 2–3% of cancer mortality is explained by obesity (86).

**Table 1-4** Increased Body Fatness and Increased Cancer Risk

Site of Cancer	Convincing Evidence	Probable Evidence	Suggestive Evidence
Esophagus	√		
Pancreas	√	Abd	
Gallbladder		√	
Liver			√
Colorectum	√, Abd		
Breast (postmenopause)	√	Abd	
Endometrium	√	Abd	
Kidney	√		

√ = increased body fatness is linked to an increased risk of cancer at the site indicated on the left. Column headings indicate the strength of the evidence linking body fatness to cancer risk.

Abd = increased abdominal fat, specifically, is linked to the increased risk of cancer at the site indicated on the left. WCRF/AICR Report, *Food, Nutrition, Physical Activity, and the Prevention of Cancer: a Global Perspective*. Washington, DC: American Institute for Cancer Research, 2007 (10).

### Nonalcoholic fatty liver disease

Obesity is the most common risk factor associated with nonalcoholic fatty liver disease (NAFLD), a condition in which normal liver architecture is disrupted by the presence of fat. The condition can progress to nonalcoholic steatohepatitis (NASH), in which there is inflammation and injury to the liver cells, which can progress to fibrosis and cirrhosis. A very high proportion of severely obese patients who have undergone bariatric surgery (surgical treatment of obesity) have evidence of either NAFLD or NASH (87). In adults, the prevalence of NAFLD or NASH is unclear (3), but indirect evidence, based on liver transaminase levels and **alanine aminotransferase** levels from NHANES, suggests it may be as high as 7.9% (88), with prevalence increasing in both children (89) and adults (90). Estimates of the prevalence of NAFLD in obese children range from 22.5% to 52.8% (91–92).

### The metabolic syndrome

The metabolic syndrome is described as a “constellation of risk factors” including central adiposity, low high-density lipoprotein levels, high circulating triglycerides, increased blood pressure, and impaired fasting glucose (93). The usefulness of the metabolic syndrome as a distinct diagnostic entity is controversial (94–95), but

there is little doubt that an increasing number of metabolic and cardiovascular risk factors confers an increased risk of morbidity and mortality. One analysis of NHANES data showed that 27% of US adults met the criteria for the metabolic syndrome (96), an ominous development from a health and economic standpoint. Using criteria adapted for adolescents (97), another analysis of NHANES data (1988–94) for 12–19 year olds showed that 30% of obese youth met the criteria for the metabolic syndrome, whereas fewer than 1% of children in the normal weight category (< 85th percentile) did (98). With an estimated 17 million teens living in the US in 2010 (99), these data suggest that the number of adolescents with the metabolic syndrome is approaching 1 million.

### Health-related quality of life

Obesity affects not only health, but other aspects of the quality of life. Obese individuals face discrimination in securing jobs, in career advancement, and even in university entrance, as discussed in detail in Chapter 2. They tend to develop a poorer self-image than their lean counterparts and often have difficulty managing social interactions. This can create stress, which may in turn lead to increased body weight and central adiposity (7).

Health-related quality of life (QOL) is defined by the WHO as including physical, mental, and social well-being (100). Instruments for measuring QOL in adults (101), adolescents (102), and children (103) are now available and suitable for use in epidemiological studies (104). Williams and colleagues conducted a prospective, longitudinal study of >1,400 primary school children (age 9–12 years) living in Victoria, Australia, and found that health-related QOL declined as weight category increased from normal weight to overweight to obesity. In clinical populations, such declines in QOL related to increased weight are also seen and tend to be even steeper (105).

Many workers have identified a relationship between obesity and depression, anxiety, and other psychological dysphorias, but most data are cross-sectional, raising the question of what comes first, the depression or the obesity. One longitudinal study (106) of 776 subjects examined the development of depression and anxiety disorder in both male and female adolescents 9–18 years of age. Using the > 95th percentile for age and sex as the definition of obesity, these workers found that adolescent obesity in females was strongly predictive of subsequent depression and anxiety, assessed by means of structured diagnostic interviews, but it was not predictive in males (106). The reasons for this striking sex difference deserve further study.

An interesting perspective on depression is provided by Ladwig and colleagues (107), who examined the con-

tribution of depressed mood in obese subjects to the risk of a future coronary heart disease event. This was a prospective, population-based **cohort study** involving three independent cross-sectional surveys of more than 6,200 subjects, of whom 737 males (23%) and 773 females (26%) were obese. The subjects were 45–74 years of age and apparently free of CHD, stroke, and cancer at the start of the study. During the mean seven years of follow-up, 179 CHD events occurred in men and 50 in women. The results showed a more than doubling of risk for CHD among men who were both obese and judged to be depressed using a standardized questionnaire. The data for women were in the same direction, but failed to reach statistical significance, perhaps because the study was underpowered (107).

Relying on self-reported data, a study of 15- and 17-year-old Swedish students, the majority of whom were from one county, found a significant statistical association between obesity and depression (108). These workers found an association between obesity and “experiences of shame,” which they defined as experiences of being “downgraded or ridiculed” by others (108). These workers concluded that shaming experiences, along with other family problems such as parental separation and parental socioeconomic factors, largely accounted for the increased rates of depression in this nonclinical population.

In ethnic minority populations, data are scant. One small but high-quality study using measured BMI and a validated instrument for measuring QOL in 175 overweight Mexican American adolescents concluded that QOL was significantly lower in the heaviest teens (109). More research is needed to examine QOL among ethnic minorities, and in all overweight children, regardless of ethnicity, interventions to improve QOL are pressing. The relationship between obesity and psychosocial functioning is discussed further in Chapters 2 and 11.

### **Mortality**

The pharmaceutical industry is aggressively developing new medical treatments for the comorbidities of obesity, and new surgical treatments (bariatric surgery, hip and knee replacements, etc.) are making a positive contribution to health status and prolonging the life of obese individuals. Nonetheless, obesity is associated with an increased risk of mortality, primarily mortality from cardiovascular disease (110–111) and diabetes (53). The relationship between BMI and mortality can be described as a U-shaped curve, with most studies showing the nadir of the curve associated with a BMI range of approximately 18.5–24.9 (112–116). This corresponds to the currently accepted definition of the healthy BMI range.

Many studies of obesity and mortality have added to the confusion regarding the exact nature of their relationship because of a failure to control for smoking or pre-existing illness, both of which increase mortality for lean persons (7). Another source of the confusion is the inappropriate control for hypertension and elevated glucose levels, which are very often effects of obesity, leading to analyses that underestimate the association of obesity and mortality (see side bar). These factors may explain why some workers have found that, in older adults, the association of BMI with mortality is either weak or nonexistent (117–118), whereas the WHO has concluded that obesity raises the risk for premature mortality “well into the ninth decade of life” (7).

Although there is continued disagreement about the risk of premature death associated with increased BMI and about how that risk differs with age, there is no disagreement that severe obesity is strongly predictive of an increased risk of premature death. The WHO reported that severe obesity (BMI  $\geq$  40) is associated with a 12-fold increase in mortality among young adults aged 25–35 (7). One study of almost 5,000 Native American children followed for several decades shows that obese children are more likely to die prematurely (before age 55) from illness and self-inflicted injury than their normal-weight peers. The death rate among the obese children was more than double that of the leanest children (141). The prevalence of obesity may be leveling off, but severe obesity is increasing in both adults and children, afflicting approximately 17 million people (41) in 2006. There is no doubt these people will face an increased risk of both morbidity and premature mortality making this an urgent public health concern Box 1-2.

### **Economic consequences of obesity**

Assessments of the economic costs of obesity have been few, and this is an area in which more research is needed. There is no doubt that overweight and obesity and their associated health problems have a significant economic impact on the US healthcare system. Costs associated with overweight and obesity are usually broken down into two categories: direct and indirect costs (142–143). Direct medical costs include preventive, diagnostic, and treatment services, pharmaceuticals, physician and surgeon costs, hospital costs, etc. Indirect costs relate to both morbidity and mortality costs; the former include the value of income lost from decreased productivity, restricted activity, absenteeism, and bed days. Mortality costs are the value of future income lost because of premature death.

In one study of national costs attributed to both overweight and obesity, the authors used the 1998 Medical Expenditure Panel Survey (MEPS) and the 1996 and

**Box 1-2 Obesity and mortality—historical perspective and current controversy**

The life and medical insurance industries were the first to investigate the relationship of body weight to risk of disease and, particularly, death. In the two largest of these studies, the Build and Blood Pressure Study of 1959 (119) and the Build and Blood Pressure Study of 1979 (120–121), a J-shaped curve of mortality was described, with persons at low and high weights showing the greatest mortality risks. In the 1959 Build Study, mortality was 42% higher in obese persons, with obesity defined as a weight 30% or more above the median weight for individuals of the same height and sex. The results of this study were used to develop a set of tables of ideal weight for height for adults. Twenty years later, because of secular increases in weight in the US population, the 1979 Build Study revealed that the lowest mortality in men under 50 years of age was associated with weights 5–15% lower than the average weights of men at that time. In men, as age increased the optimal weights for the lowest mortality increased somewhat, but were still below the earlier range defined by the 1959 Metropolitan Life Tables. For women, the weights associated with lowest mortality increased with increasing age, suggesting that older individuals could safely be somewhat heavier. But it was also noted that the rise in mortality for obese individuals became steeper as excess weight increased.

Since the Metropolitan Life Tables guided clinical practice for decades by defining ideal or healthy weight-for-height, it is worth noting some limitations of the life insurance data on which the tables were based. They were primarily gathered from Caucasian, upper- and middle-income persons and as such were not representative of the US population as a whole. In an effort to address these limitations, the American Cancer Society (ACS) initiated a long-term longitudinal study in the general population (122–123). The results of this study, conducted between 1969 and 1972 on 700,000 people, were similar to the two Build studies. This suggested that the data obtained from the insurance pool population could be extrapolated to the general population. All three studies found the lowest mortality at weights below the population average (119–120, 122–123), suggesting that the distribution of weight in the US was shifting to higher levels and was associated with a shorter lifespan. Because the ACS was especially interested in cancer, it separated smokers from non-smokers, which the insurance studies had not done. Smoking is an independent risk factor for premature mortality and smokers tend to be leaner than nonsmokers. Since the two Build studies included smokers, they overstated the risks of being underweight and understated the mortality risk of being obese (119–120, 124).

In 1984, Waaler and colleagues (125) reported on an extensive longitudinal study carried out in Norway. The lowest mortality was found in the BMI range of 23–25. In the younger male age groups, mortality began to rise more steeply at a BMI of 29. In women, the lowest mortality was in the BMI 23–27 range, and increased gradually above that.

The Framingham study was another longitudinal investigation, using a sample of the population of a typical

middle-class American town. This study also showed the lowest mortality occurred at weights that were 5–15% below the average weight of the population (126). Two other longitudinal studies, in which subjects were followed for 34 and 26 years, respectively, showed a significant independent effect of obesity on mortality (127–128).

The Nurses' Health Study (63), now in its 18th year, is following more than 100,000 US women to define the association between a number of factors and mortality. The nurses ranged from 30 to 55 years of age at the start of the study. These workers reported a significant association between BMI and mortality in a subpopulation that carefully excluded smokers. The lowest mortality was found at a weight at least 15% below the average weight for US women of similar age. The relative risk of dying prematurely from heart disease in non-smoking women began to rise at a BMI of 22, but reached statistical significance at a BMI of 27, and was 7.7 times higher than the normal weight control group at a BMI > 32. The relative risk for all-cause mortality in non-smoking women also began to rise at a BMI of 22 and was 2.2 times greater at a BMI > 32. Thus, this study confirms that overweight and obesity increase the risk of premature mortality in women, as had been previously reported for men in the Framingham study (126).

Although many studies indicate a strong relationship between obesity and mortality, a number of studies have not found a relationship between the two (129–139). There are at least two possible explanations for this. First, mortality studies must be of long enough duration so that the absolute number of deaths suitable for analysis is high enough to provide sufficient statistical power to detect differences. In studies where different age groups are studied, this can be difficult to achieve. Second, in many of the studies the very diseases that are associated with or exacerbated by obesity have been eliminated or controlled for. For instance, diabetic patients have been excluded from most studies; hypertensive persons have either been excluded or blood pressure controlled in analyses. Because obesity exerts much of its effect through such conditions, the elimination of these comorbid conditions greatly attenuates the measured adverse effect of obesity. This has been discussed by Manson and colleagues (140), who have shown that in 25 major prospective studies on the relationship between obesity and longevity, there was at least one of three biases that led to systematic underestimation of the impact of obesity on mortality. These biases are: 1) failure to control for cigarette smoking; 2) inappropriate control for the biological effects of obesity, such as hypertension and hyperglycemia; and 3) failure to control for the presence of subclinical disease. The latter is usually controlled for by discarding mortality data for the first 3–5 years of the study in the event that those deaths were attributable to pre-existing disease that was undetected at the start of the study. These are some of the factors identified by the WHO, which reviewed the evidence on this issue and concluded that obesity raises the risk for premature mortality "well into the ninth decade of life" (7).

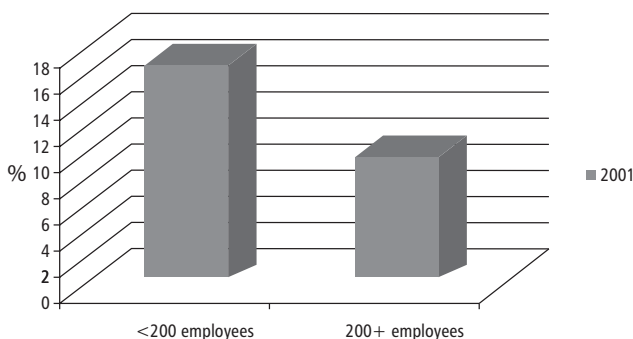


1997 National Health Interview Surveys (NHIS) to estimate direct medical costs. The data also included information about each person's health insurance status and socio-demographic characteristics. This estimate of the costs of overweight and obesity combined amounted to as much as \$78.5 billion, with \$47.5 billion attributable to obesity alone, with Medicare and Medicaid financing roughly half of these costs (144).

When the costs of overweight and obesity are adjusted for inflation and the data expressed in 2008 dollars, the direct costs of obesity reach as high as \$147 billion (145). It is estimated that this represented almost 10% of all medical spending in the US in 2008 (145). Finkelstein and colleagues have estimated the costs of obesity at the state level, where costs range from \$87 million (44% covered by Medicare and Medicaid) in Wyoming to \$7.6 billion (45% covered by Medicare and Medicaid) in California (146). It is worth noting that in 2009 the CDC budget specifically for the Division of Nutrition, Physical Activity and Obesity (DNPAO) for addressing obesity at the state level is insufficiently funded so that only 23 states are funded by the DNPAO for fiscal year 2009.

The cost of private insurance is usually shared by employers and individual workers, and is increasingly identified as a sharply increasing business cost that is forcing some employers to withdraw health insurance for their employees. The majority of people who are privately insured obtain their insurance through their employer and the majority of employed persons regard health insurance as their most important job benefit (147). But the cost of health insurance is rising rapidly, especially for employers who employ fewer than 200 employees (see Figure 1-8).

The consequence is that smaller employers are forced to drop health insurance coverage for their employees, or they shift the costs—via higher premiums or co-pays—to their employees. Figure 1-9 illustrates the data for the years 2000–2.

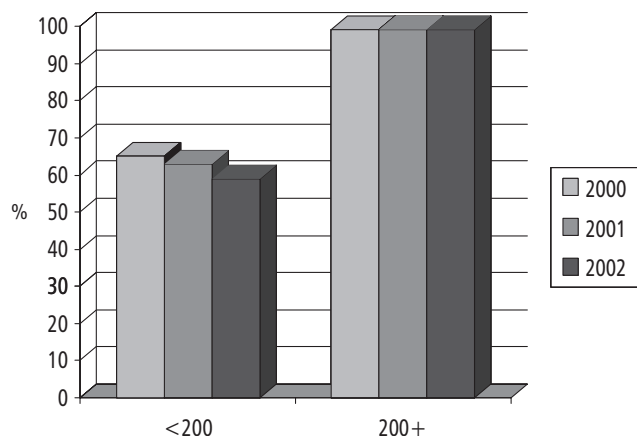


**Figure 1-8** Percent increase in costs of health insurance to employers, by size of workforce

In the US, corporate CEOs and state and federal political leaders are decrying healthcare costs which soared from \$73 billion in 1970, to \$253 billion in 1980, to \$714 billion in 1990, to \$2.1 trillion in 2006 (147–148). These costs amount to more than \$7,000 per resident and account for 16% of US gross domestic product (147–148). The high prevalence of chronic illnesses has been identified as one of the major factors driving healthcare costs. Other factors are long-term care services, such as nursing homes, prescription drugs, and assistive or therapeutic technology, the aging of the population, and escalating administrative costs. Except for administrative costs, as shown in Box 1-3, obesity plays an important role in each factor identified, although there is a great need for future research to provide more specific quantitative information.

One Fortune 500 company recently documented a 19 cent reduction in earnings per share directly attributable to rising healthcare costs (149). According to one source, since 2001 employees are paying 64% more in healthcare costs and employers are paying 78% more (150). Indeed, the coffee giant Starbucks has 80,000 employees and in 2005 was reportedly spending more on health insurance than on coffee beans (151).

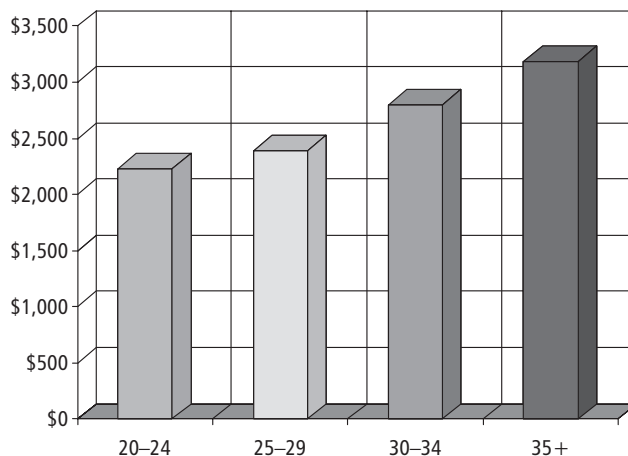
A number of workers have examined the linkage between obesity and rising healthcare costs. Quesenberry and colleagues (152) studied obesity and the cost of health services utilization among more than 10,000 respondents to a 1993 health survey of members of a large health maintenance organization in northern California (152). The results (shown in Figure 1-10) indicated that the mean annual cost per person was 25–33% higher in obese persons—these additional costs amounting to as much as \$500–1,000 per year (in 1993 dollars).



**Figure 1-9** Percentage of firms offering health benefits, by size of workforce

**Box 1-3 Obesity and Increased Healthcare Costs**

Factor Driving up Healthcare Costs	Role of Obesity in that Factor
Increased chronic illness	Obesity itself is a chronic condition and leads to the development of many other chronic conditions (diabetes, heart disease, hypertension, certain cancers, etc.)
Aging of the population	The prevalence of obesity steadily increases from age 20 to age 55 in males; and from age 20 to age 75 in females (see Health, United States, 2006; Table 73)
Prescription drugs and technology	Drugs are used to treat obesity and its comorbidities; the use of new technology such as lap-bands, etc., in bariatric surgery and prosthetic devices in joint replacement surgery
Long-term care services, such as nursing homes	Greater joint problems lead to decreased mobility and reduced health in older obese individuals, resulting in increased need for nursing home stays



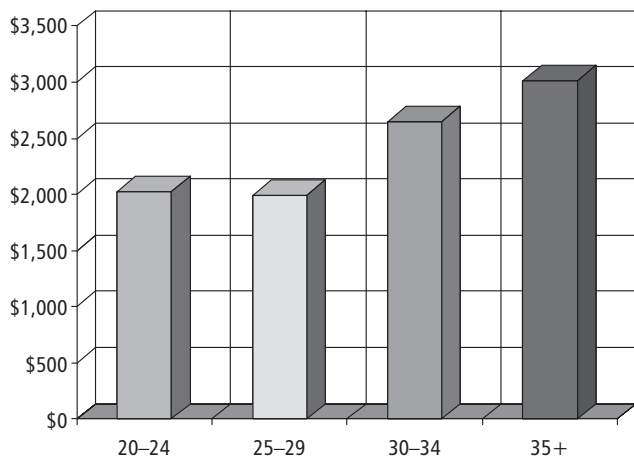
**Figure 1-11** General Motors study 1996–1997: 177,000 indemnity/PPO participants, median medical costs

reflecting a growing sentiment that prevention is cost-effective whereas treatment may not be.

A similar study of a large manufacturing population by Wang and colleagues and colleagues (153) also demonstrated progressively higher healthcare costs with increasing BMI. As shown in Figure 1-11, they reported a difference in annual costs of approximately \$1,000 between normal-weight individuals and those with a BMI of 35 or higher.

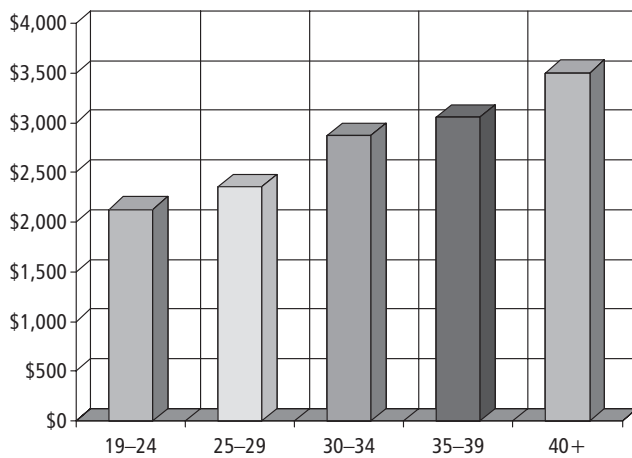
Anderson and colleagues (154) examined healthcare costs associated with physical inactivity, overweight, and obesity among members of a Minnesota-based health plan. An insufficient number of members self-identified as non-White, so the analysis was limited to Whites aged 40 and older. Mailed surveys (response rate 79%, final  $n = 4,674$ ) permitted collection of data on physical activity, height, weight, chronic disease, smoking, age, and sex. These data were linked to administrative health claim data and included professional fees and hospital claims, but not pharmacy charges. The cost data were standardized to 1997 US dollars. These workers found that 23.5% of healthcare costs incurred by this population were associated with physical inactivity, overweight, and obesity. Further analyses suggested that the figure, nationally, for persons 40 and older was even higher—27% (154).

To translate this finding into dollars for a hypothetical health plan with 200,000 members aged 40 and above, total costs would be \$1.12 billion, of which \$263 million (23.5%) would be associated with physical inactivity and overweight or obesity—a conservative figure (see discussion of drug costs below), since it does not include pharmacy costs (154). A surprising finding was that 75% of healthcare costs (\$197,500) attributable to physical inac-



**Figure 1-10** Kaiser Permanente (n > 10,000) health services utilization: mean annual cost per person by BMI

These authors suggested that given the high prevalence of obesity and the data on increased rates of health services use and costs, a promising strategy to reduce healthcare expenditures would be through obesity prevention efforts. It is notable that they emphasized prevention rather than stepping up efforts to treat obesity,



**Figure 1-12** National data on health care expenditures by BMI, white females 35–44 years old, 2003 dollars

tivity and overweight or obesity were incurred by men, who comprised only 44% of the population (154). This finding suggests the importance of designing population-level strategies to promote physical activity and stem overweight and obesity that are appealing to men aged 40 and older.

Wee and colleagues (155) used national 1998 Medical Expenditure Panel Survey (MEPS) data to examine the relationship between healthcare expenditures and BMI. MEPS is a national longitudinal survey funded by the Agency for Healthcare Research and Quality (AHRQ) (see [www.meps.ahrq.gov](http://www.meps.ahrq.gov)) which relies on self-reported data on healthcare expenditures, as well as demographic, insurance, and other information cross-validated with records kept by medical providers, insurers, and pharmacies. As shown in Figure 1-12, these workers found a similar stepwise relationship between BMI category and costs in White women. Interestingly, these workers found no relationship between BMI and healthcare costs among Hispanics and Blacks. This might be explained by the small number of study subjects who were Black (i.e., insufficient power), but another factor cited by the authors was inferior access to and quality of healthcare and competing health risks and other causes of death for minority groups (155).

An important finding in this study was that annual healthcare expenditures rose in a stepwise fashion with increasing BMI for all age groups older than 35 years. These workers noted that the relative rise was more substantial as adults increased in age, so the difference in dollars spent between obese and normal-weight individuals was nil in persons 18–34 years old, approximately \$700 per year in persons 35–54 years old, and more than \$2,000 per year in persons 55 years and older. The cost

spread in women age 55 and older was even greater—approximately \$3,000 per year (155). These workers found that obesity was associated with higher costs in all major categories of care: hospital services, outpatient services, prescription medications, office visits, and emergency room visits (155). They singled out prescription medications, since obesity led to the largest relative rise in expenditures in this category, and suggested that this could mean that obesity is driving the rise in drug costs in the US. This observation may be relevant to another study, described below.

Over the next two and half decades, the number of people older than 65 will increase by 50%, predicting a precipitous rise in obesity-related health costs (155) associated with the aging of the population. According to the WHO, the estimated direct cost of obesity is comparable to that of other prevalent chronic diseases, such as type 2 diabetes and coronary heart disease, and is more costly than both hypertension and stroke (7). Moreover, obesity contributes to the development of other chronic diseases; it is estimated that 61% of the direct cost of type 2 diabetes, 17% of the direct cost of coronary heart disease, and 17% of the direct cost of hypertension are attributable to obesity (7).

### Costs of severe obesity

According to Finkelstein and Brown (156), 9% of the full-time US workforce is eligible for bariatric surgery. These severely obese (usually defined as a BMI of 40 or above) members of the workforce lose 5.1 additional days of work and incur more than \$2,000 in excess medical costs each year compared to their normal-weight counterparts. Pregnancy in the severely obese is particularly costly because of the higher rate of pregnancy complications, caesarean delivery and premature birth that requires placement of the infant in intensive care. At one hospital in New York City, it was estimated that the cost of pregnancies with those complications exceeds \$200,000 as compared to \$13,000 for a normal delivery (157).

Only a small proportion of those eligible actually seek bariatric surgery for the treatment of their obesity. Barriers that have been identified are lack of physician referrals, outmoded understanding of the various types and associated risks of bariatric procedures, and lack of insurance coverage for surgery. Bariatric surgery is a method of reducing food intake by reducing the size of the stomach to a tiny pouch, a procedure that usually involves rearranging the intestine to bypass the small intestine (see Chapter 19). The majority of patients lose 50–75% of their excess body weight within two years and keep most of it off over the long term. The procedure is costly to perform (see below) and requires a lifetime of

follow-up, especially for patients with more than one obesity-related comorbidity prior to surgery, who face a higher risk of post-operative complications (158). One study of 2,522 surgeries at 308 hospitals found that, in the first 180 days postoperatively, the readmission rate was 18.2% and the total six-month risk-adjusted health-care payments were \$65,031 in readmitted patients versus \$27,125 in those without readmission (158). Between 0.5% and 1.5% of patients die in the hospital (159) after the operation—a mortality rate that may not apply currently, as more and more hospitals and surgeons start bariatric surgery programs (160). In one study, researchers examined regional differences in severe obesity and bariatric surgery rates, as well as risk factors for death after surgery. They identified nearly 70,000 patients who underwent the surgery in 2002 (161) and found that 85% were women and 76% were 18–49 years old. Interestingly, these workers found that the prevalence of severe obesity was lowest in the North-East and West and highest in the Mid-West and South (162). However, the rates of bariatric surgery per 100,000 severely obese individuals ranged from a low of 139 in men aged 60 and older in the Mid-West to a high of 5,156 in women aged 40 to 49 in the North-East (162).

Identifying appropriate candidates for bariatric surgery is crucial. In a study of nearly 55,000 adults who underwent bariatric surgery in 2001, Poulouse and colleagues (159, 161) found that being male or being older than 39 approximately doubled the risk of postoperative mortality. Patients insured through Medicaid faced a nearly five-fold greater risk, and those requiring additional surgery faced a more than 20-fold greater risk of postoperative death (159). These data emphasize the critical importance of appropriate patient selection, although other factors such as the number of procedures performed each year not just by the surgeon, but by the entire surgical team, are thought to be very important.

There is every reason to believe that the number of procedures performed each year will continue to rise as hospitals around the nation launch bariatric programs. The 2001 Surgeon General's Report on Overweight and Obesity concluded that the economic costs of obesity exceed \$100 billion annually (163). As mentioned earlier, in 2008 direct costs alone were estimated to be nearly 50% higher than that figure (145). Total economic costs of obesity (which would include both direct and indirect costs) are likely to be more than double that amount given the tremendous increase in the number of persons with a BMI of 40 or above since 2001 and the escalating number of hip and knee replacement surgeries due to overweight as well as the increased number of bariatric

surgical procedures that cost between \$10,000 and \$40,000 and require a lifetime of medical follow-up.

An emerging picture of significantly higher medical costs among the obese will not necessarily result in greater advocacy for obesity treatment since treatment of obesity is in itself costly. One analysis, supported by AHRQ, on the cost-effectiveness of **gastric bypass** for severe obesity concluded that this procedure is cost-effective when compared to the cost of no treatment, and provides substantial lifetime benefits (164). But AHRQ commented that since the reduction in lifetime medical cost was not greater than the cost of treatment, "gastric bypass was not cost-saving from the payer perspective." An analysis by Heinen (149) focused on a large employer in the North-East who discovered that 85% of its 35,000 employees were overweight or obese. If just under half of those employees qualified for drug treatment, Heinen calculated it would cost \$1,800 per person or \$27 million per year for an obesity "drug that is prescribed indefinitely" (149). Studies such as these present a dilemma as to how to help people who are already obese lose weight, since the price tag for treatment can be high, especially when treatment involves costly drugs, medical services, surgery, and healthcare professional monitoring, and the success rate for nonsurgical treatment is reportedly low. Although the data are clear that for severe obesity bariatric surgery is effective and can produce sustained weight loss, the cost of such surgery is high, especially when the costs of postoperative complications and lifetime follow up are factored in. Furthermore, surgery is not an appropriate choice for overweight people and perhaps not for obese people with a BMI of 30–40, although there is controversy regarding the threshold of BMI at which surgery is appropriate. There are lower-cost alternatives to surgery, such as the commercial Weight Watchers program and the noncommercial TOPS (Take Off Pounds Sensibly) program, but success rates of such programs are usually unknown and the training of service providers may be inadequate (7). The continued growth of such programs, which were established in the US approximately 50 years ago, suggests that the model of trained laypersons delivering responsible weight-loss information and providing ongoing weight management support may well be a cost-effective approach that could be evaluated for its utility in community settings. Such an approach is being used at the community level to increase physical activity and found to be cost-effective (165). In January 2007, the state of West Virginia Medicaid program announced that it would begin providing free access to Weight Watchers to an estimated 75,000 eligible obese persons (166). This approach is being attempted in 14 other states and the

results will be of great interest to the public health community, once they are available.

Taken together, the data presented above should galvanize employers to forge partnerships with health insurance providers to prevent weight gain among their normal-weight and overweight employees—and carefully examine their stake in addressing childhood obesity prevention, especially family-based approaches to treatment. Prevention and treatment of childhood obesity is not just right for the sake of protecting the health of children; it may also make good economic sense, although this remains to be demonstrated. Stemming healthcare costs associated with obesity depends on building a constituency for prevention, especially a strategy for the prevention of childhood obesity that engages parents as well as other adults, as we strive to insure a healthy and competitive workforce in years to come.

### The etiology of obesity

Throughout most of human history corpulence was viewed as a sign of social status, health, and prosperity. For most people, a lifetime of hard physical labor, marked by daily struggles to secure a sufficient amount and variety of food, was the common lot. Rural areas in third world countries such as India, where obesity is rare, demonstrate that the abundance and variety of affordable food available in all seasons of the year and the widespread ability to earn a living without physical exertion are relatively recent phenomena. These are the benefits of technology, sophisticated agricultural techniques, and rapid transportation, supply, and distribution networks that are still largely confined to first world countries and to rapidly modernizing urban centers in the third world.

It may seem odd to consider the etiology of obesity, when it may appear obvious that the cause is simply over-consumption of calories relative to the amount of calories needed for the maintenance of a healthy weight. But it is puzzling that some people seem to balance their food intake to match their energy expenditure without giving the matter much thought, whereas for others it is a constant struggle. It is equally puzzling that some people embrace physical activity with enthusiasm, while others make every effort to avoid it. The nature of the battle to control weight differs in subtle ways from one person to another. For some, the problem may be increased appetite and overeating, whereas for others, the issue is a sedentary lifestyle in which there is no necessity for physical activity. Perhaps for most of us, the challenge lies in both domains—the domain of excess

energy or calorie consumption, and the domain of insufficient energy expenditure, primarily through low levels of physical activity.

This section will address a variety of etiological factors that have been posited as favoring the development of obesity. It is offered from the point of view that no single factor is responsible for the development of obesity. Rather, many factors favor a positive energy balance, but the contribution of each is small and difficult to measure. If 0.45 kg of fat is roughly equivalent to 3,500 kcal, a positive energy balance of only 35 kcal a day leads to a weight gain of 0.9–1.35 kg a year. This translates to an increase of one BMI unit approximately every two years. Under this hypothetical scenario, a decade is sufficient time to move from a BMI in the normal range to the obese range. Consequently, it is the identification of all factors that favor positive energy balance that is the appropriate focus of our efforts to stem obesity. A few of these factors will be discussed below.

### *The Big Two: eating and exercise*

From a practical standpoint, there are only two avenues to weight control that an individual can influence—how much is consumed (i.e., food and drink) and how much physical activity engaged in. These are referred to as the Big Two (167). It has rightly been pointed out that the environment, broadly defined to include the family, community, school, workplace, marketplace, built environment, and the entire cultural and socioeconomic context in which an individual lives, can profoundly influence the Big Two.

From the perspective of thermodynamics, body weight changes are a function of energy balance: weight gain occurs when energy intake exceeds energy expenditure, and weight loss occurs when energy expenditure exceeds energy intake. Energy is expended through three basic pathways: 1) resting metabolic rate (RMR), which is the energy expended to carry out bodily functions while the body is at rest, including the repair and maintenance of cells and tissues, the maintenance of resting heart rate, a constant body temperature, and other physiological processes needed to maintain a constant internal environmental and hormonal milieu; 2) the thermic effect of food, which is the excess heat generated when food is consumed, digested, and absorbed; and 3) physical activity, which is variable and the only component of energy expenditure that is subject to voluntary control (7).

The largest component of energy expenditure is RMR, which usually accounts for 60–70% of total daily energy expenditure (TEE) (168). The thermic effect of food accounts for approximately 10%. The energy expenditure associated with physical activity is dependent on the

amount and nature of the physical activity one engages in. In a highly active individual, energy expended through physical activity might be as high as 40% of TEE, but it might be as little as 10% of TEE in a sedentary individual. Thus, for countries such as the US and UK in the 20th century, or China and India in the 21st, shifting from a primarily agricultural economy in which hard physical labor is common to a more technologically advanced, information-based economy in which it is not, the population will undergo a large reduction of energy expenditure, with perhaps as much as 600–1,000 fewer kcal expended per person per day. As physical activity levels decrease, appetite and calorie intake will spontaneously reduce as well (see Chapter 8), but other factors, such as the availability of inexpensive, highly palatable foods may interfere with this physiological down-regulation by stimulating food intake and preventing perfect compensation. This may explain the weight gain commonly observed under these circumstances (169–170). We will begin by considering the taste and palatability of foods which, evidence suggests, promote overconsumption.

### **Taste, food palatability, and overconsumption**

The food industry is well aware that the single most important driver of food selection and consumption is taste. The taste and palatability of a new food product will be carefully tested on members of the market segment for whom the food is intended. The WHO has identified palatability as “one of the most powerful influences” on feeding behavior, which acts by increasing the rate of eating, as well as the sense of hunger during and between meals (7). (See Chapter 8 for more information on the regulation of appetite.)

A major contributor to the palatability of food is fat, which provides a pleasant “mouth feel” (as in ice cream) and is an excellent vehicle or carrier for flavors, which is why it is used in sauces and gravies. But fat contains more than twice as many calories per gram as either carbohydrate or protein, and is therefore a major contributor to the energy density of foods, even as it contributes to their enhanced palatability. This may be a factor favoring positive energy balance, because, if an energy-dense food is consumed quickly, a large number of calories can be consumed before satiety has a chance to develop and the meal is terminated (171–172).

A particularly palatable combination is fat and sugar, such as found in cupcakes, butter cookies, fudge, and so on. Drewnowski identified combinations of fat and sugar as highly appealing to humans, and perhaps more appealing to obese women (171) than to their lean counterparts. Savory snack foods are formulated as highly palatable combinations of fat and salt that interact with

taste receptors on the tongue and stimulate neural signals to the brain that “feed forward” to encourage further consumption. This feed-forward concept is succinctly captured in the Madison Avenue slogan for a popular snack chip: “Bet you can’t eat just one!”

For an individual whose daily maintenance energy (calorie) needs are 1,800kcal, the NHANES dietary intake data show that nearly 600kcal are devoted to energy-dense, nutrient-poor foods, with two likely consequences: 1) it is a challenge to deliver a healthy diet and meet essential nutrient needs within the remaining 1,200kcal; and 2) overeating is likely for the reasons discussed above. In this sense, the consumption of a high-fat, highly palatable diet can establish and perpetuate the obesity epidemic without delivering optimal nutrition.

Unlike the storage capacity for protein and carbohydrate, which is very limited, the body’s storage capacity for fat is virtually unlimited. Since fat’s palatability and limited satiating capacity encourage overconsumption, a surfeit of dietary fat is a common occurrence. The human body does not respond to this physiological challenge of excess fat consumption by increasing fat oxidation as a compensatory mechanism. Fat oxidation is generally proportionate to fat mass. So the physiological response is a slow expansion of fat stores (assuming calorie balance is positive); fat oxidation will slowly increase as fat stores expand until fat oxidation finally matches fat intake. But balance is achieved at the cost of a higher level of obesity. In summary, fat is especially fattening because it is the most energy-dense component of our diet and thus promotes a positive energy balance; in addition, it promotes its own consumption and it fails to stimulate its own oxidation (173–176).

The widespread availability and affordability of a tasty, high-fat diet is a remarkable achievement of the 20th-century food, agriculture, transportation, and distribution industries, but it favors a positive energy balance in a sedentary population such as the US population. Ready availability is buttressed by astute advertising and merchandising strategies that encourage product trial. Further, the products are carefully formulated by food manufacturers to maximize their instant appeal to consumers (177). The WHO has specifically suggested that lower fat intakes (in the range of 20–30% of energy) may be needed to minimize energy imbalance and weight gain in sedentary individuals (7). How to achieve this reduction in fat intake on a population basis is a tremendous public health challenge, but large clinical trials to prevent diabetes (54–55) suggest that reductions in fat intake help produce and sustain weight loss over a period of several years and translate into significant reductions in disease risk.

## Sugar-sweetened soft drinks and soda

The possible role of soda or soft drinks and other sugar-sweetened beverages in the development of positive energy balance is a matter of great interest. A meta-analysis of 88 studies (178) found associations of soft drink intake with increased energy intake and increased body weight. But not all studies have implicated soda as a cause of obesity. Vartanian and colleagues (178) suggested that study design significantly influences the results. Larger effect sizes were found in studies using a stronger experimental design (i.e., longitudinal and experimental studies). Studies of weaker design (i.e., cross-sectional or observational studies) were less likely to find an association. Thus, these workers concluded that population-based strategies to prevent childhood obesity by limiting soft drink consumption are “strongly supported” by the available scientific evidence.

In fact, only two of the 88 studies analyzed by Vartanian and colleagues (178) were designed to directly test whether reductions in soda consumption would lower BMI. One study by James and colleagues (179) designed a special curriculum to reduce soft drink consumption in 644 children aged 7–11 years old in six primary schools in south-west England from August 2001 to October 2002. After one year, the percentage of overweight and obese children increased in the control group by 7.5% and decreased in the intervention group by 0.2%. This study has been criticized primarily because the documented decrease in soft drink consumption was very small (~50 mL per day) and was of insufficient magnitude to explain this finding.

The second study was an intervention by Ebbeling and colleagues (180) conducted during the 2003–4 academic year. This was a small study of 103 subjects aged 13–18 years, who were daily consumers of at least 12 oz of soft drinks or other sugar-sweetened beverages. The subjects were randomized into two groups and calorie-free soda was delivered to the homes of the intervention subjects for 25 weeks. Control subjects were asked to continue usual beverage consumption habits for 25 weeks. Consumption of sugared soft drinks decreased by 82% in the intervention group and was unchanged in the controls. Change in BMI was not different between the two groups as a whole. However, an analysis of the heaviest subjects in the two groups showed a greater beneficial effect of reduced sweetened soda consumption in the intervention group as compared to the heaviest subjects in the control group (180).

Because of the complexity of obesity and the many factors contributing to overweight, there is a low likelihood that a single change will have a beneficial effect on weight gain, perhaps explaining the equivocal findings

described above. Nevertheless, the findings of these two interventions support the notion that soda consumption favors a positive energy balance. Future studies of the value of reducing soft drink consumption as just one component of a multi-component prevention strategy should be pursued as a high priority.

## Supersizing and portion control

Researchers have documented the increasing portion sizes offered on a routine basis to US consumers, including children (181). Wansink has characterized portion size as one of the many external cues that encourage overeating and favor a positive energy balance (182) (see Chapter 6). Developmental data support this notion. Although infants are born with the ability to self-regulate their food intake, somewhere between the ages of 3 and 5 years that ability can be overridden by the presentation of large portion sizes, which will encourage them to eat, apparently in the absence of hunger (183). Studies of the effects of portion size on the food intake of adults have documented a similar response. Adults will eat more when larger portions are offered (184). Furthermore, larger plates and bowls and larger serving spoons encourage them to serve larger portions and eat more as a consequence (185; see Chapter 6).

Supersizing is not just the marketing of a large portion of a food. It is an example of a marketing strategy that offers a highly attractive “added value”—a larger quantity of a tasty food—for little or no incremental cost. The consumer sees the supersized portion of food as a “good value” because the cost increment is negligibly small. Hence, the supersized portion appeals on a rational economic basis—because it is a bargain—as well as from a taste perspective. Supersized menu choices often are available in food establishments that are designed to appeal to children and their busy parents in many important ways: 1) the taste of the food is carefully crafted to appeal to children and adults alike through the strategic use of ingredients such as fat, salt, and sugar; 2) the economic value of supersized portions is appealing to those on a restricted food budget and to those who appreciate good value regardless of their budgetary constraints; and 3) the convenience of such restaurants, many of which have drive-up window service or even a home delivery service that eliminates virtually all the time and trouble associated with planning, shopping, preparing, and cleaning up after meals. From a food industry perspective, a great deal of emphasis is being placed on the development of convenience foods for the US consumer. The appeal of convenience foods may involve a number of possible factors (see below), but this is an area in which more research is needed.

Convenience factors that have been identified are 1) the parental time famine (186), which leaves little time for meal planning, shopping, preparation, and clean-up; 2) marketing, which casts cooking as drudgery and presents purchased meals as cheaper and better than what can be made at home; 3) parental attitudes that each family member should be able to choose when and what to eat; and 4) cultural changes which have promoted TV time and TV dinners over family time and the family dinner (187).

One interesting new tool designed to help researchers and program developers evaluate the nutritional features of foods as well as the pricing and promotion strategies of retail food outlets (restaurants, convenience stores, and grocery stores) is the Nutrition Environment Measurement Survey (NEMS) (188–189). Although it requires training, NEMS can be used by laypersons to document the use of supersizing and other promotions that encourage the purchase of large portions that favor overeating. Work has begun to use NEMS data as the basis of programs designed to improve the nutrition environment in a community setting (190).

### Physical activity

Physical activity exerts a powerful influence on the physiological regulation of body weight, partly because it is the major component of total energy expenditure that is under volitional control. Thus, increases in physical activity will boost energy expenditure and favor a negative energy balance. An additional beneficial adaptation of the human body to routine physical exercise is the enhanced capacity to preferentially oxidize fat. This means that physically trained individuals will oxidize more fat at a given level of energy expenditure than will an untrained individual. In other words, enhanced fat oxidation is a training effect; as much as a 20% increase in fat oxidation was documented in initially untrained individuals after a 12-week fitness training program (191). This suggests that routine exercise sufficient to become physically fit will help maintain body weight not only by burning calories but also by specifically enhancing fat oxidation.

This finding led other workers to examine whether the ability to handle dietary fat would differ depending on an individual's customary level of physical activity. Stubbs and colleagues (175) found that sedentary individuals consuming a low-fat (20% of calories) diet *ad libitum* remained in energy balance whereas the same individuals consuming a 40% fat diet *ad libitum* were in positive energy balance and stored the excess energy as fat. Moderate physical activity changed this by permitting *ad libitum* consumption of a 40% fat diet, without favoring a positive energy balance or fat storage (175).

These results are certainly not an invitation to consume a 40% fat diet, which is unlikely to be heart-healthy in any event, but they do suggest that a low-fat diet favors the maintenance of energy balance, even in sedentary individuals. In physically fit people, slowly increasing the level of fat in the diet will, at some point, overwhelm the body's capacity to increase fat oxidation. Where this threshold lies in response to increases in exercise is not known and will likely vary from person to person, as the degree of training will also vary, but this needs to be verified experimentally.

Other factors such as insulin secretion will likely modify this picture. Using a proxy measure of insulin secretion, Chaput and colleagues (192) showed that a high first-phase insulin concentration (measured at 30 minutes after administration of a 75 g oral glucose load) predicts both gain in weight and waist circumference over six years in adults, especially among those consuming "lower-fat" diets.

A disappointing aspect of this study, as in so many studies of the effects of diet on weight gain and adiposity, was a failure to control for physical activity levels or fitness. The natural experiment in Cuba described earlier showed that the Special Period was characterized by several years of a low-fat, high-carbohydrate "diabetogenic" diet, accompanied by very high levels of physical activity, which resulted in significant weight loss and improvement in diabetes and heart disease mortality (49). In the Special Period, the intake of calories was limited by circumstances, whereas in the Chaput study (192) diet was not controlled, and in fact the mean changes in body weight and waist circumference did not differ between the lowest- and highest-fat diet groups (192). If we are ever to determine the optimal diet composition for minimizing weight gain at all relevant levels of physical activity, an urgent research need is for researchers conducting diet studies to control for physical activity and for all exercise studies to control for diet (193).

### Energy flux and the maintenance of energy balance

An issue rarely receiving research attention is whether balancing food intake against energy expenditure is somehow more difficult to achieve at lower levels of energy flux. Consider the professional athlete who routinely eats and expends 4,000 kcal a day and then retires from sports. His energy expenditure drops precipitously and, although his food intake decreases as well, he is no longer in energy balance and begins to steadily gain weight. Does the weight gain that usually accompanies such a change occur because balancing energy intake (i.e., food intake) against energy expenditure is more difficult at this new lower level of energy flux? This ques-



tion is particularly important in children. If children are much more sedentary today than 20 years ago, as has been reported (194–195), they need to regulate body weight at a lower level of energy flux. Gutin (196), for example, studied 500 adolescent children using **accelerometers** to determine activity levels and 24-hour recalls to assess diet. He found that vigorously active individuals had the highest calorie intake, yet were significantly leaner than their less active counterparts who were consuming fewer calories (196). That obesity has become more prevalent in children of all ages is indisputable, as the data discussed above illustrate, but the possibility that the rise in obesity is a consequence of a mismatch of intake and expenditure that occurs more commonly and more readily at low levels of energy flux is intriguing. Since the regulation of energy balance appears to be facilitated by high levels of vigorous, rather than moderate, activity in children (196), promoting vigorous physical activity in youth may be a critical refinement of public health messages and strategies targeting youth.

In adults, public health messages to promote 30 minutes of daily physical activity are now well established, but the level of activity is carefully described as “moderate” and is an “evidence-based” message that relates to good health. For most people, however, 30 minutes of moderate physical activity will not prevent the weight regain that often follows weight loss, nor is it likely to prevent weight gain, especially if overconsumption of foods and caloric beverages is a routine practice.

### **Other factors identified as putative contributors to obesity**

#### **Pharmaceutically induced weight gain**

Aronne has helped raise awareness of the many drugs that induce weight gain and the need to carefully evaluate the possible undesirable consequences of the gain against the therapeutic benefit, especially in cases where other options are available (197) (see Chapter 23). Keith and colleagues (167) have provided a convenient review of the wide range of drugs that produce weight gain and the list is impressive for its length and also for the wide range of disorders for which these drugs are prescribed (see Table 1-5).

These workers identified several potential contributors to obesity that were known to have changed over the past 30 years, the period corresponding to the sharp increase in prevalence of obesity in the US, including the sales and use of the compounds on this list (167). Clearly, the weight gain associated with these drugs is an unintended consequence of their use, but one that may understandably deter patient compliance. There seems little doubt that the widespread use of a wide variety of drugs is a likely contributing factor to the obesity epidemic.

**Table 1-5** Drugs that Produce Weight Gain

Pharmaceutical Agent	Comments
Psychotropic medications (antipsychotics, antidepressants, mood stabilizers)	Many of these cause significant weight gain
Anticonvulsants	Promote weight gain
Anti-diabetics	Insulin, sulfonylureas promote weight gain; thiazolidinediones promote adipocyte proliferation
Anti-hypertensives	Beta-blockers induce mean weight gain of 1.2 kg
Steroid hormones and contraceptives	Data inconsistent on contraceptives
Antihistamines	More potent compounds produce weight gain
Antidepressants	Produce weight gain; data for selective serotonin reuptake inhibitors inconsistent
Atypical antipsychotics	Olanzapine and clozapine produce as much as 4 kg over 10 weeks
HIV antiretroviral drugs	Produce weight gain and abdominal adiposity

Ref. (167).

#### **Sleep debt**

The possibility that sleep debt is a contributor to the obesity epidemic has gained currency in recent years (198–199). It has been suggested that, in humans, sleep debt has a harmful effect on carbohydrate metabolism and endocrine function, and induces changes in hormones such as **leptin** and **ghrelin** (198, 200). Lopez-Garcia and colleagues (201) conducted a prospective study, from 2001 to 2003, of >3,500 older adults using self-reported data on sleep duration. These workers found that sleeping for 5 hours or less or sleeping 8 or 9 hours (but not 10 hours or more) was associated with obesity, but not abdominal obesity (201), resulting in a roughly U-shaped relationship (if one ignores the  $\geq 10$  hour finding) between hours of sleep and obesity. Similar findings have been reported in younger adults (201) and in a population aged 30–102 (202).

Taheri has recommended that greater care should be taken to ensure that children get sufficient sleep to prevent obesity (203). Supporting this recommendation

is a study of more than 8,500 four-year-old children showing that ensuring that children get adequate sleep (10.5 hours or more per night) was one of three household routines associated with childhood obesity prevention (see Chapter 27 for more information). In children from homes supporting all three household routines, a 40% lower prevalence of obesity was observed as compared to children exposed to none of these routines (204). The TV and other forms of recreational screen viewing (including texting on phones) interfere with sleep in a variety of ways; the location of TVs, videos, DVDs, and cell phones in the bedroom invite late-night phone calls and screen viewing that can delay bedtime or interrupt sleep. The content of shows can cause nightmares and delay the onset of sleep or cause sleep disturbances (205). Understanding how sleep may be connected to obesity is an area in which more research is needed, in both adults and youth.

### Urban vs. rural

*Rural Healthy People 2010* (206) reported that individuals living in rural areas are more likely to be obese than residents of urban areas, but studies are few. Jackson and colleagues (207) used BRFSS data for the years 1994–96 ( $n = 342,055$ ) and for 2000–1 ( $n = 385,384$ ) to estimate the prevalence of obesity in rural areas and to describe trends. The data were organized into urban or rural categories based on county codes available on BRFSS. The rural category was further subdivided based on distance from a large metropolitan area or a town with  $\geq 10,000$  residents. The data showed that, overall, obesity prevalence was 20.5% in urban areas, but rural areas adjacent to large metropolitan centers had a 23.5% prevalence, sparsely populated rural areas had a prevalence of 23.3%, and more densely populated rural areas had a prevalence of 21.1% (207). These urban/rural differences were statistically significant and the differences were smaller but remained significant after the data were adjusted for other demographic factors. States with the highest rates of obesity in all types of rural counties combined were Mississippi, Texas, and Louisiana (207). These workers noted interesting patterns in obesity prevalence with respect to education. In urban areas, obesity prevalence declined substantially as years of education increased: prevalence among the college-educated was 5.1% lower than for those without a high school diploma. This gap narrowed to only 2% in sparsely populated rural areas. This finding suggested the possibility that options for preventing and reducing obesity are “less accessible” in rural than in urban counties (207). They also reported substantially higher obesity prevalence among African Americans and also for American Indians living in rural counties, suggesting the need for culturally tailored interventions (207).

It is important to recall that BRFSS relies on self-reported height and weight to calculate BMI and does not include institutionalized individuals or individuals living without a telephone, the latter being a potentially important limitation in rural areas. Regrettably, these workers did not examine or control for physical activity levels, which are available through BRFSS. But they cite the work of others (208–209) showing that rural residents are less likely than urban or suburban residents to meet recommendations for physical activity. Another issue not discussed is the quality of the foods available in grocery and convenience stores as well as restaurants in rural areas. Preliminary research (190) suggests that this lack of readily available produce and other nutritious foods of low energy density may also be a contributory factor in accounting for urban/rural differences in obesity prevalence.

### Socioeconomic status and race/ethnicity

In general, the literature suggests that in developed countries there is an inverse relationship between socioeconomic status (SES) and obesity prevalence, whereas in developing countries it is the higher SES populations who are at higher risk for obesity (210–214). Fewer studies of the relationship between obesity and SES in children and young people have been reported, and fewer still examine how race and ethnicity may change that relationship.

Wang and Zhang (215) examined secular trends in the relationship between obesity and SES, using NHANES data from 1971 to 2002 for 30,417 children aged 2–18 years. The ratio of household income to the poverty threshold varies with household size and other factors, and thus these workers divided the ratio data into “Poverty income ratio” tertiles to indicate low, middle, and high SES. Significant differences by race, sex, and age were observed. These workers observed an inverse relationship between SES and obesity only in White girls. In other groups, the relationship was direct. African American children of high SES were at increased risk (215).

A more recent study by Freedman and colleagues (216), using NHANES data from 1999 to 2004, also found that White children of high SES were at decreased risk for obesity and that Mexican American children had a similarly decreased risk with high SES. Among Black children, however, the two studies showed that obesity is positively associated with SES (215–216).

There is a strong similarity in the obesity–SES relationship for 6–11-year-old children and 12–18 year olds within each ethnic group (216). Whites and Mexican Americans are most similar to each other; in these two ethnic groups, obesity prevalence goes down as SES goes up in the two age categories. For Blacks, obesity prevalence increases with SES and that holds true for both 6–11 year

olds and 12–18 year olds (216). Delva and colleagues (217) present similar data from the Monitoring the Future study from 1998 to 2003, a study of 39,000 students in the 8th and 10th grades. Again, the pattern of decreasing overweight prevalence with increasing SES was observed in White and Hispanic youths, but not in Blacks (217).

It is important that Wang and Zhang (215), who examined secular trends, comment that overall the association between obesity and SES is weakening, at least in the US. They also suggest that efforts to target income disparities will probably not reduce racial disparities in obesity (215). Delva and colleagues (217) examined self-reported behaviors associated with overweight and suggest that differences in lifestyle behaviors and family characteristics may help to explain the racial/ethnic differences in obesity prevalence. They urge the development of policies and programs to address the greatest need among minorities and low SES groups (217).

Caballero studied 1,704 young ( $7.6 \pm 0.6$  years) school children living in seven American Indian communities and found a very high prevalence of obesity in both boys (26.8%) and girls (30.5%) (218). Anderson and Whitaker have shown striking ethnic disparities in obesity prevalence in children as young as four years old (219). In their study of 8,550 children who participated in the Early Childhood Longitudinal Study Birth Cohort, overall prevalence of obesity was 18.4%, with prevalence varying by race or ethnicity as shown in Table 1-6.

Research focused on lowering overall prevalence of obesity and eradicating these stark ethnic disparities in prevalence is an urgent public health need.

### Maternal and paternal obesity transmission to offspring

Whitaker has shown that paternal obesity is associated with a doubling of the risk of obesity in the offspring; maternal obesity is associated with a four-fold increased risk, and obesity in both parents is associated with a 10-fold increased risk (37). (Chapter 9 provides more infor-

mation on parental effects on childhood obesity.) For practical reasons, most studies of the effects of pregnancy on childhood obesity concentrate on maternal rather than paternal characteristics and their effects on obesity transmission. It is estimated that nationally one in five women are obese when they become pregnant (220–222; see Chapter 10). However, in some regions of the US, the proportion is much higher. For example, at Maimonides Medical Center in Brooklyn, NY, 38% of the women giving birth are obese (223). There is a direct relationship between the extent of overweight in parents and the transmission of obesity to their offspring (224–227). Thirty years ago, childhood obesity was considered transient—children would usually grow out of it. It is now viewed as persistent, that is, the presence of obesity in childhood predicts obesity in young adulthood (37) and is now known to be associated with increased health risk (see Chapter 11). Studies of surgical weight loss in severely obese women prior to pregnancy show that treating severe obesity improves the course of pregnancy and the development of the offspring born to surgically treated mothers. Comparison of postoperative to preoperative pregnancies in the same mothers showed that after the surgery the course of pregnancy is marked by greater insulin sensitivity, improved lipid profile, and a 52% reduction in the prevalence of offspring obesity (228–230). These studies document reduced complications for the mother, fetus, and newborn infant such as reduced rates of preeclampsia, gestational diabetes, caesarean delivery, prematurity, and birth defects. But the important finding we emphasize here is a reduced prevalence of childhood obesity in the offspring, suggesting the vital importance of targeting females of childbearing potential to prepare them for a healthy pregnancy through the achievement and maintenance of a healthy body weight at conception and throughout their childbearing and parenting years.

### Reproduction and the fat-brain axis

Although recent data suggest that the prevalence of adult obesity may be starting to plateau (231), many women are now entering pregnancy obese, and it has been shown that pre-pregnancy maternal (and to a lesser extent paternal) obesity is associated with a significantly higher risk of childhood obesity in their offspring (37). An increasing number of women of all ethnicities around the world are obese when they become pregnant. Since maternal obesity rates continued to rise from the 1980s to the present, we will not see the full effect of maternal obesity on obesity rates in children until maternal obesity rates stabilize.

Excessive weight gain during pregnancy, weight retention between pregnancies, and failure to breastfeed may

**Table 1-6** Obesity Prevalence in Four-Year Old Children, by Race/Ethnicity\*

American Indian/Native Alaskan	31.2%	**
Hispanic	22.0%	**
Non-Hispanic Black	20.8%	**
Non-Hispanic White	15.9%	**
Asian	12.8%	**
Overall	18.4%	

\*Based on data from (219).

\*\*Statistically significant from all other ethnic groups ( $p < 0.005$ ).

all be factors contributing to the obesity epidemic. These factors will be considered in detail in Chapter 10. It is noteworthy that cultural factors may play an important role. For example, Vallianatos and colleagues (232) examined the beliefs and practices of **First Nation** women (Cree women in north Quebec) about weight gain during pregnancy and breastfeeding practices. These workers found that the women acknowledged the health consequences of excessive weight gain but cited a number of barriers to controlling weight gain, such as lack of time, beliefs about diet, lack of child care, and a paucity of programs for new mothers (232).

Catalano (233–235) has postulated that the presence of maternal insulin resistance and a chronic inflammatory condition associated with maternal obesity may play a role in the rising prevalence of obesity. Normal pregnancy is considered an insulin-resistant state, but obesity, especially obesity with underlying insulin resistance, may alter the hormonal milieu for the developing fetus to selectively favor fetal fat deposition. Elevated fat stores in the fetus would raise fetal leptin levels that shape feeding centers in the hypothalamus, altering neural development to favor increased appetite and a positive energy balance.

A normal infant is born with a fully developed capacity to experience hunger and responds by eating to satiety. Bouret and colleagues (236) have suggested that the hormone leptin affects both neuronal activity and synaptic plasticity in the **arcuate nucleus** of the hypothalamus, playing a **neurotrophic** role during a critical period of fetal brain development. This region of the hypothalamus is thought to house two populations of neurons with opposing actions on food intake (see Chapter 8). One population stimulates and the other suppresses food intake (237). Whether this obtains in humans remains to be demonstrated, but it is possible that an enlarged fetal fat mass, driven by the insulin-resistant state prevailing in the obese mother, produces elevated levels of leptin and other hormones that drive the developing hypothalamic fetal appetite regulatory system toward a positive energy balance.

In their review of possible causes of obesity, Keith and colleagues (167) presented evidence that maternal age (i.e., the age at which women bear children) is increasing globally. They suggest that this secular trend might produce a clinically meaningful (approximately 7%) increase in the odds of obesity. The above scenario is but one possible explanation of how this might occur. The possibility of expanded fat stores in the fetus and newborn is troubling in light of increasing environmental exposure to fat-soluble hormones and toxicants that may influence metabolism and the eventual development of obesity comorbidities. Keith and colleagues

(167) discuss endocrine disrupters and other possible intra-uterine and intergenerational phenomena that may be at play, including the possible influence of adenovirus-36 (167).

A particularly interesting study of the development of obesity and the metabolic syndrome in an animal model suggests a possible role for the microbiota in the gastrointestinal tract (238). These workers point out that the development of obesity is associated with a shift in the relative abundance of the bacterial phyla colonizing the gut, possibly causing a shift in the innate immunity of the organism and a decrease in metabolic health. Toll-like receptor 5 (TLR5) is a transmembrane protein that is highly expressed in the intestinal mucosal cell and is capable of binding bacterial flagella. Mice that are genetically deficient in this receptor show signs of an inflammatory state and are heavier and fatter than their wild counterparts, with a particular increase in visceral fat. The deficient mice show substantial increases in serum lipids and blood pressure, mild elevations in blood glucose, elevated basal insulin levels, and loss of glycemic control. When high-fat fed, they displayed hepatic steatosis (fatty liver) and other signs of insulin resistance. When food intake is restricted, many of these changes normalize (238). A crucial finding in these studies is that transfer of the gut microbiota from the deficient mice to wild-type germ-free animals established the hyperphagia, obesity, hyperglycemia, insulin resistance, and elevated levels of inflammatory markers in these new hosts, suggesting that host–microbiota interactions may play a fundamental role in the development of the hyperphagia and obesity (238). These findings warrant further investigation for their relevance to human obesity and the development of the metabolic syndrome.

With one third of the US adult population obese, the growing prevalence of obesity in women of childbearing age may be predisposing the next generation to enter their childbearing years in the obese state, creating a self-perpetuating cycle of maternal and child obesity (233). It has long been known that excessive thinness and excessive obesity are both associated with infertility, but even so Keith and colleagues (167) have raised the possibility that women with higher BMI may have greater fecundity and higher reproductive fitness, which they define as “one’s capacity to pass on one’s DNA” (167). They also suggest that “assortative mating,” in which phenotypically similar individuals are more likely to mate with one another, may result in a higher rate of individuals with higher BMI mating with each other. Whether they pass on obesity to their offspring through a combination of genetic and environmental factors (since parents provide both to their offspring), the result is increasing prevalence of obesity over time. This vicious cycle of events

provides an entirely new rationale for addressing parental, perhaps especially maternal, obesity as a cornerstone of childhood obesity prevention, and may represent an important strategy to stem the obesity epidemic.

One especially interesting study of the effects of maternal obesity on childhood obesity was conducted by Kral and colleagues (228–229). These workers compared the prevalence of obesity among 172 children who were born to surgically weight-reduced mothers ( $BMI = 31 \pm 9 \text{ kg/m}^2$ ) and 45 age-matched siblings born to severely obese mothers ( $BMI = 48 \pm 8 \text{ kg/m}^2$ ) prior to surgery. In children born after maternal surgery, the prevalence of obesity decreased by 52% (with no increase in the prevalence of underweight) and prevalence was reduced to population levels. The authors suggest that their results demonstrate the importance of “potentially modifiable **epigenetic** factors” that need to be identified and characterized (229). Since severe obesity, such as that present in these mothers prior to their bariatric surgery, is considered by some to be under genetic control, the findings of Kral and colleagues (228–229) raise important questions about what that really means with respect to the obesity epidemic.

### Genetics

According to the WHO, the rapid increase in obesity rates in recent years has occurred “in too short a time for there to have been any significant genetic changes within populations” (7). They suggest that the focus should be on “environmental and societal changes” that have “overwhelmed the physiological regulatory processes that operate to keep weight stable in the long term” (7). Others disagree (239), citing numerous studies in the literature suggesting possible changes in the genetic background of contemporary populations by factors such as assortative mating, increased fecundity of moderately overweight persons, demographic changes in a population, and epigenetic effects (239). (See Chapter 5 for more information on the genetics of obesity.)

Misunderstandings arise from how the heritability of obesity is discussed and understood by scientists and how it is represented in the media. Coverage often reflects the “all-or-nothing” view of the issue (240), whereas the actual science is complex and nuanced. The risk of widespread ignorant or irresponsible media coverage is that individuals or entire populations will regard their current weight, BMI, or waist circumference as inevitable and unchangeable, which may then translate into a fatalistic view of their current and future health.

The twin method of studying the heritability of obesity depends on comparing the manifested (**phenotypic**) similarity or dissimilarity of genetically identical (i.e., monozygotic) vs. genetically non-identical (i.e., fra-

ternal or dizygotic) twin pairs. The differences between within-pair correlations observed in groups of the two types of twins provide us with an estimate of the contribution of the heritability of a trait—that is, a measure of the extent to which the phenotypic (manifested) variation in a trait such as obesity is genetically determined. Remaining phenotypic variation in this trait is attributed to environmental factors (241). There are studies comparing twins (identical and fraternal) reared apart to those reared together, and these provide additional information about the effects of genetic inheritance as compared to the effects of environment.

Published adult twin and adoption studies have found that variation in BMI was largely due to heritable genetic factors and the heritability estimates in these studies range from 55% to 85% (241). Twin studies have yielded the additional insight that most of the environmental influences on BMI come from unique influences (non-shared environmental effects), rather than from the shared family context.

Wardle and colleagues (241) observed that most twin studies have been conducted in adults and speculated that shared environment effects (family influences) may be stronger in pediatric samples. They also sought to study a pediatric sample born after the onset of the obesity epidemic (241). These workers reported that BMI and abdominal obesity, as indicated by high waist circumference, have a high heritability factor, as high as 77% for BMI. They found that environmental effects are small and are roughly equally divided between shared and not-shared environmental effects (241). It is noteworthy that the authors of this study still recommend targeting the family for obesity prevention in the earliest years, and suggest that “longer-term weight control” will require both “individual engagement and society-wide efforts to modify the environment,” clearly indicating their belief that the current obesity epidemic can be addressed, despite the high heritability of both BMI and central adiposity (241). To explain what may appear to be a paradoxical position, the authors provide the example of phenylketonuria, a genetic disease that is entirely heritable which is nonetheless treated by an environmental intervention, specifically a phenylalanine-free diet. This illustrates the important point that although a trait such as BMI or central adiposity is highly heritable, it does not justify a fatalistic view that nothing can be done to address the problem.

### Conclusion

Obesity is an increasingly prevalent and costly problem in the developed and developing world. It carries health risks for the populations affected, and increases

morbidity and mortality to such an extent as to present a very significant public cost. The etiology of obesity has been difficult to untangle, but there is clearly a genetic component to acquiring excess weight. The genetic susceptibility of an individual seems to be fully expressed in environments in which food is tasty, variable, plentiful, cheap, and widely promoted, and in which technology has replaced human physical labor in most aspects of endeavor. While the genetic mechanisms involved have begun to be unraveled, obesity in most cases is likely to be a polygenic disease in which numerous genes interact to facilitate obesity to develop when the environment is permissive.

Although studies are lacking, it may prove to be more cost-effective to prevent weight gain than to lose weight once obesity occurs. Without proof that this proposition is true, it is clear that prevention is viewed as the answer to this great public health problem, as it has been for the last five decades (242). Yet it is important to bear in mind that there is no natural constituency for obesity prevention, which is costly, as there is for obesity treatment, which is also costly, but represents a business opportunity for a number of industries. The industries that can view obesity treatment as an opportunity include pharmaceutical manufacturers, dietetic food and beverage manufacturers, weight loss services, and surgical device manufacturers, to name just a few.

Building support for prevention as a national priority requires an increased awareness of the health risks and costs associated with obesity and of the health advantages of increased physical activity, wholesome food choices, and healthy weight. A change in lifestyle is necessary for most Americans, the motivation of which is currently not well understood. It will likely require awareness of the dangers of obesity and embracing a healthy weight as a desirable and shared cultural value with a view to establishing it eventually as a cultural norm.

One factor militating against lifestyle change is the delay in onset of the negative consequences of obesity. It is difficult to change behavior if the desired outcome or benefit is many years in the future and that benefit is the absence of the development of a disease. To persuade an individual to change behavior now to prevent an event 10–20 years in the future is not easy. It requires a clear awareness of the health risks of obesity and acceptance that lifestyle change is possible, which is now missing in most population groups. It also requires the identification, availability, and affordability of solutions that will facilitate change.

Public education will be necessary, much as public education about tobacco was necessary to decrease its

use. But food is more difficult to limit than tobacco, and physical activity is noxious to many people, especially as they get older. At a 2008 national summit on obesity prevention and control sponsored by the CDC (243), 10 factors were identified as targets for obesity prevention efforts (see Box 1-4). The first six are identified as “behavior target areas that form an evidence-based framework to prevent and control obesity” (244). The last four are additional areas in the social domain that “require attention to appropriately address the social impact of obesity” (244).

This book offers the reader valuable information on each of the target areas for obesity prevention that the CDC has identified. Indeed, this book can be viewed as a tool that will inform and, we hope, galvanize readers who will help us pave the way toward the CDC vision of “[a] world where regular physical activity, good nutrition, and healthy weight are part of everyone’s life” (245).

#### Box 1-4 Targets for Obesity Prevention Efforts

1. Reducing consumption of “energy-dense” or high-calorie foods.
2. Reducing consumption of sugar-sweetened beverages.
3. Increasing consumption of fruit and vegetables.
4. Increasing the initiation and duration of exclusive breastfeeding.
5. Reducing screen-time (TV, movies, computers, video games).
6. Increasing physical activity across the lifespan.
7. Increasing development and dissemination of guidelines for physical activity and physical education standards.
8. Improving societal responses to the causes and condition of obesity, including reducing stigma and discrimination and improving disparities in priority indicators among population subgroups.
9. Reducing disparities in access to healthcare services for obese persons (e.g., medical coverage for obesity-related health conditions and treatment, durable medical equipment to conduct regular and routine exams, education and information dissemination to healthcare providers).
10. Reducing barriers to obesity prevention and control (e.g., consensus-building on the definition and classification of obesity as a disability and/or disabling condition) (244).

### Summary: Key Points

- Obesity is the result of a sustained imbalance between energy (or calorie) intake and energy (or calorie) expenditure. Multiple factors contribute to this imbalance.
- Body mass index is the ratio of weight, expressed in kilograms, to the square of height expressed in meters ( $\text{kg}/\text{m}^2$ ). It correlates with body fat content.
- For estimating obesity prevalence in populations, BMI is used in adults and the age- and sex-specific BMI percentile is used in children (2–20 years).
- In the US, obesity prevalence is estimated based on either self-reported or measured height and weight in national surveys.
- About one third of adults and nearly 20% of children in the US are obese.
- Obesity comorbidities are disease conditions that develop or worsen as weight increases and improve with weight loss.
- Chronic diseases associated with obesity include several leading causes of premature death in the US: heart disease, diabetes, and certain cancers.

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