Textbook of Obesity
Companion website: Textbook of Obesity

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• Extensive bank of Questions and Answers
• All figures from the book for downloading
• Note-taking outline for each chapter
• Webliography
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While I served as U.S. Surgeon General from 1981 to 1989, the data from the National Health and Nutrition Examination Survey (NHANES) and the Behavioral Risk Factor Surveillance System (BRFSS) documented a surge in obesity prevalence in America. The data spurred me to found the nonprofit organization, Shape Up America! in 1994, to raise awareness of obesity as a health issue. The prevalence of obesity has continued to climb with upsurges documented in adults and children in all walks of life, with the problem more severe among America’s poor and uninsured.

Progress in raising awareness of obesity as a health issue has certainly been made, but there has been little progress in stemming the epidemic. We now have nearly 75 million Americans categorized as “obese” and more than 17 million are categorized as “severely obese.” Of greatest concern, an estimated 12 million children are obese with 2.5 million severely obese.

Now we are learning that the offspring of obese and severely obese parents are at greater risk of obesity, introducing a new understanding of the way the obesity epidemic is self-propagating through epigenetic pathways. With so many millions of Americans of childbearing potential entering pregnancy and parenthood in the obese condition, this represents a deepening of the crisis.

A broadly increased understanding of the many causes and consequences of obesity is urgently needed. The field has made remarkable strides enlightening us about the endocrine function of fat cells and how leptin—a protein synthesized by fat cells—crosses the blood-brain barrier to mediate the communication between body fat depots and regulatory centers in the brain that influence appetite and energy balance. But much more work needs to be done, particularly to develop effective prevention and treatment approaches.

The publishing world is highly competitive and up to now, a comprehensive textbook such as this one did not exist. The editors and authors of this volume have labored for more than 3 years to create a textbook suitable for college level students and those who are beginning their graduate education. Their goal was to attract bright new minds to the field of obesity to help us devise innovative research, invent new medical devices, discover new therapeutic agents for treatment, and develop public health solutions to help us stop and reverse the epidemic. I am proud to support their effort as I share their hope that making information about the complex nature of obesity more accessible to students will increase the likelihood of finding urgently needed answers to these highly perplexing problems.

Now I am calling upon you, the reader, to help us move the field forward and make America a healthier place to live, learn, work and play. There is no doubt that it takes a nation to stem obesity and regardless of your chosen career path, we call upon you to be a part of the solution.

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Sharon R. Akabas, Barbara J. Moore and Sally Ann Lederman

A major theme of this book is to understand the complexity of the factors that underlie energy balance and weight, with the goal of understanding the overweight or obese person. Understanding is an attribute I have had modeled for me my whole life, by my parents, Eli and Rebecca Freedman, and my siblings, Karen Jimmerson, Jay Freedman, Barry Freedman, Beth Rosen, Jayne Quinn, Judy Fask, and Barbara Freedman. This modeling has been continued in my own family by my husband, Myles, and children, Sam, Leor, and Reuben. I am grateful to all of them for their love, humor, support, and patience during this arduous process.

Sharon R. Akabas

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Sally Ann Lederman

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Barbara J. Moore

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α-melanocyte-stimulating hormone(s); alpha-MSH
A set of peptide hormones secreted by the anterior pituitary gland. In the brain, release increases appetite.

2003 Rotterdam criteria Criteria used to define PCOS established during a conference of experts who met in Rotterdam in May 2003 and indicate that PCOS can be diagnosed (once certain other conditions are excluded) when two of three conditions are present: infrequent or no ovulation, indications of hyperandrogenism, or polycystic ovaries. These criteria expand the definition of PCOS established by an April 1990 expert conference sponsored by NIH.

95% confidence interval An estimate, determined from the standard error, of the range of values for a given variable that would include the true mean 95% of the time. It is used to indicate the reliability of the estimate of the mean provided by a particular sample. Greater sample sizes reduce the range of the confidence interval, making the estimate of the mean more reliable.

acanthosis nigricans A darkening and thickening of the skin usually seen at the nape of the neck and in areas where opposing skin surfaces can touch and rub, such as in the groin, underarms, and beneath pendulous breasts; associated with insulin resistance.

accelerometers An instrument for measuring acceleration, used in some methods that determine energy expenditure. Initiation of movement in a part of the body involves an acceleration, which can be counted, if registered on the accelerometer. Complex models are used to convert these counts into calories expended, using a variety of estimates and assumptions.

activity thermogenesis Energy expenditure above that used when at rest.

acute phase reactants Proteins whose concentration in the plasma are changed significantly during inflammation.

ad libitum An amount of food freely chosen by an individual; unrestricted food intake.

adaptive immune responses An immune response dependent on action of antigen-specific lymphocytes.

This response can result in lifelong protection from reinfection with the same antigen.

adipocyte A connective tissue cell containing one or more fat droplets. The adipocyte is the defining cell type within adipose tissue; also known as “fat cell.”

adipogenesis The formation of fat; fat cell proliferation.

adipokines Any of a variety of compounds secreted by adipose tissue; some play important roles as signaling molecules in energy balance and metabolism.

adiponectin An adipokine, a protein hormone secreted by adipose tissue. Has generally beneficial effects on insulin-sensitive tissues and the vascular system.

adjusted odds ratio An odds ratio statistically adjusted for other factors that might affect the chance of the disease. See odds ratio.

adrenal hyperandrogenism Excessive production of androgen hormones (testosterone, dehydroepiandrosterone, etc.) by the adrenal glands.

adrenalectomy Removal of the adrenal gland.

afferent centers Areas of the brain that integrate signals from the body and send outgoing (efferent) messages via neural pathways to other parts of CNS and to other parts of the body.

agouti protein A protein produced in the body (endogenous) that has a strong stimulating effect on appetite. It acts as an antagonist of the melanocortin receptors MC3R and MC4R.

air displacement plethysmography A method for determining body volume. It consists of two connected chambers in one of which the subject is placed, the other being a reference chamber that contains pressure-measuring instruments. A flexible diaphragm is mounted in the common wall between the chambers. The ratio of the pressures in the two chambers as the diaphragm is moved is inversely related to the ratio of the air volumes within the chambers, allowing calculation of body volume.

Akt One of a set of protein kinases with various functions, including apoptosis and insulin signaling.
alanine aminotransferase (ALT)  An enzyme found in the plasma, liver, and other tissues; it catalyzes the conversion of alanine to alpha-ketoglutarate by transfer of an amino group. Elevated blood levels are used as a indicator of liver damage.

alimentary limb  In bariatric surgeries, the portion of the remaining intestinal tract that carries food.

alkaline phosphatase  An enzyme made in liver, bone, intestine, and kidney. If levels are elevated in blood, it suggests liver disease or damage or bone problems.

alternative complement pathway  A part of the immune system that does not depend on the action of antibodies. It kills pathogens quickly, before antibody synthesis can occur. It operates by the binding of a protein, complement protein C3b, to the pathogen surface.

anatomical bony landmark  Protuberances on the bones that can be used to identify specific anatomical locations on the body surface.

androgen receptor  A receptor that is activated by binding androgen hormones (hormones that determine male secondary sex characteristics).

angiogenic  Relating to the formation of new blood vessels.

angina pectoris  A feeling of pain or pressure in the chest, often radiating to the arms, neck, or back, caused by inadequate oxygen delivery to part of the muscle of the heart.

angiotensinogen  A plasma precursor of angiotensin, a compound that causes blood vessels to constrict, raising blood pressure.

anorexiant  A substance that causes loss of appetite.

ANS tone  The level of activity in the autonomic nervous system.

anthropometry  Measurement of the physical characteristics of the body, such as its size, weight, shape and proportions.

antigen  Any substance foreign to the body that evokes an immune response.

antihyperglycemic agents  A substance that promotes the normalization of blood glucose levels.

apocrine odor  The odor emitted by the apocrine sweat glands, glands found mostly in the armpit and genital areas.

arcuate nucleus (ARC)  An area in the hypothalamus that contains neurons that secrete appetite-enhancing neuropeptide Y, and appetite-suppressing melanocortins, and many other substances.

area postrema (AP)  An area of the brain, on the base of the 4th ventricle, that is involved in feeding control and in vomiting.

associative learning  A learning process by which stimuli become linked together.

AST (aspartate aminotransferase)  An enzyme whose blood levels are used as a test of liver function.

attrition  The loss of participants in a study. It is usually expressed numerically as a percentage of those originally enrolled or assigned to a treatment.

autocrine  A type of cell signaling in which a cell secretes signal molecules that act on itself or other neighboring cells of the same type.

autonomic systems  The part of the nervous system that controls involuntary visceral functions such as the heartbeat, digestion, and glandular secretions. Includes the sympathetic and parasympathetic components.

autosomal  Related to any chromosome other than a sex chromosome.

autosomal genetic disorder  A genetic condition that results from a gene on an autosome (i.e., not sex-chromosome linked).

autosomal recessive disorder  A disorder that appears only in people who have two mutated copies of an autosomal gene, one from each parent.

bariatric surgery  Surgical procedures designed to reduce body weight. Different approaches will reduce nutrient absorption or decrease the amount of food that can be eaten at one sitting, or both.

beta-blockers  Drugs that decrease the heart rate and lower blood pressure by blocking cellular beta-receptors. These receptors normally are responsive to epinephrine and norepinephrine; the interaction with the drug affects heart rate and contractility, vasodilation, blood pressure and other physiological activities.

binge-eating disorder  An eating disorder involving repeated episodes of excessive overeating, feelings of loss of control and worthlessness. These are not balanced with compensatory actions to correct the excess intake, such as by fasting, vomiting, using laxatives, or exercising excessively.

bioelectrical impedance; bio-impedance analysis (BIA)  A method for estimating body composition (total body water, extracellular water) from the conductance and resistance of the body, determined by applying a small
electric current across a portion of the body (e.g., hand to foot).

**BMI growth charts** Charts produced by the CDC, used for assessing the growth of children.

**body dissatisfaction** Concerns with body shape, in particular the experience of “feeling fat.”

**body mass index (BMI)** A measure used to classify the appropriateness of weight relative to height. Calculated as weight (kg) divided by height (meters) squared. Previously called Quetelet’s Index, after Adolphe Quetelet, its developer. Used as an indicator of body fatness.

**borborygmi** The noises made when gas moves in the intestine.

**bougie** A cylindrical, tapering device used to enter a tubular part of the body, such as the esophagus.

**bromide dilution** A body composition method in which bromide is introduced into the body by injection or in a drink, and its concentration in extracellular water (ECW) is used to estimate the ECW volume. The method depends on the assumption that bromide does not leave the ECW to a significant extent over a period of a few hours.

**bulimia nervosa** An eating disorder characterized in the Diagnostic and Statistical Manual of Mental Disorder IV-TR by recurrent episodes of binge-eating followed by recurrent inappropriate compensatory behavior (e.g. self-induced vomiting, laxative abuse) to prevent weight gain. The binge-eating episodes must be characterized by both 1) eating, in a discrete period of time (e.g., within any 2-hour period), an amount of food that is definitely larger than most people would eat during a similar period of time under similar circumstances; and 2) a sense of lack of control over eating during the episode.

**BUN (blood urea nitrogen)** The portion of blood nitrogen that is in the form of urea. Used to assess kidney function.

**calcium channel blockers** Drugs used to treat abnormal rhythms of the heart and to reduce high blood pressure via vasodilation of the arteries.

**calipers** An instrument used to measure the distance between two surfaces, by positioning the calipers two “legs” or “jaws” on the surfaces, and reading the dimension from a measuring dial.

**cannabinoid receptors** Receptors in the brain that are affected by the chemical constituents of cannabis (marijuana). They have been studied for their role in appetite regulation; thus far their effects on mood have been considered too high risk and drugs affecting these receptors have not obtained FDA approval.

**cardiac valvulopathy** The condition where a valve of the heart is diseased.

**catecholamine** Hormones (including dopamine, epinephrine and norepinephrine) that increase heart rate and stroke volume, increasing blood pressure.

**CCK** See cholecystokinin.

**celiac disease** A digestive disorder resulting from inflammation of the small intestine caused by gluten, a substance found in various grains, including wheat, barley, rye, and possibly oats.

**cellulitis** Diffuse inflammation of connective tissue, especially subcutaneous tissue.

**ceramides** Naturally occurring sphingolipids where sphingosine is connected to a fatty acid. They are important in the synthesis of sphingomyelin.

**chemokines** Small, secreted, chemo-attractant proteins that stimulate the migration and activation of cells, especially phagocytic cells and lymphocytes. Chemokines are important for immune system function.

**Child Nutrition Act of 1966** A law, signed by President Johnson in October 1966, designed to improve the nutrition of school children, largely through school-based feeding programs, such as the school breakfast program, which it established.

**cholecystitis** An inflammation of the gallbladder, usually due to a gallstone.

**cholecystokinin (CCK)** A polypeptide hormone that acts as a satiety signal. It is produced in the duodenum, mostly in response to the presence of fat. It stimulates the contraction of the gall bladder and secretion of pancreatic enzymes, and inhibits gastric secretion and motility.

**cholelithiasis** The presence or formation of gallstones.

**cirrhosis** A disease of an organ, mostly commonly referring to the liver, characterized by the invasion by fibrous connective tissue, usually the result of inflammation or injury, such as from alcoholism in cirrhosis of the liver.

**classical conditioning** A learning principle in which two stimuli become paired through their repeated association with each other.

**cohort study** A form of longitudinal study where the occurrence of a disease is compared in an exposed group...
and a group without the exposure, to determine if disease is associated with the exposure.

**complement**  A system of plasma proteins that can be activated directly by pathogens or indirectly by pathogen-bound antibody, leading to a cascade of reactions that occurs on the surface of pathogens and generates active components with various effects. There are three pathways of complement activation: the classical, the MB-lectin, and the alternative.

**complete blood count**  A standard blood test that reports the concentration in the blood of the white and red blood cells, the platelets, and other aspects of blood cells, such as hemoglobin and mean corpuscular volume.

**Comprehensive Metabolic Panel**  A test that measures the blood levels of glucose and numerous electrolytes, proteins, enzymes and other compounds useful in the diagnosis of many diseases.

**computed tomography**  An x-ray imaging method that can produce three-dimensional images of the inside of the body.

**confounder**  In statistics, a variable that correlates with a disease cause and a disease outcome, but which is not itself causal of the disease. Unrecognized confounders can lead to spurious conclusions about the causes of disease.

**Continuing Survey of Food Intakes by Individuals**  This national survey of the food intake of Americans is conducted by the U.S. Department of Agriculture on a yearly basis.

**contraindication**  A condition that, if present, would preclude the use of a particular treatment under consideration.

**coronary heart disease**  Disease that results from the narrowing or blocking of the arteries that supply the heart muscles with blood.

**corpus uteri**  The main body of the uterus, below the fallopian tubes and above the place where the uterus narrows at its lower end.

**correlational studies**  Studies that examine the mathematical relations between variables. Can establish association but not causation.

**cotinine**  (in serum) An alkaloid that is a product of the metabolism of nicotine.

**counter-regulatory hormones**  Hormones that oppose the action of other hormones, such as insulin, glucagon, adrenaline, cortisol, and growth hormone. They raise the level of glucose in the blood by various metabolic pathways.

**C-reactive protein**  A protein released as a response to inflammation.

**criterion method**  A method used as a reference standard against which other methods can be validated.

**cytokines**  Non-antibody proteins secreted by inflammatory leukocytes and some non-leukocytic cells, which act as intercellular mediators. They differ from classical hormones in that they are produced by a number of tissue or cell types rather than by specialized glands. They generally act locally in a paracrine or autocrine manner.

**demographic characteristics**  Characteristics of human populations, such as race, age, SES, education and employment status, etc.

**deuterium (deuterium dilution)**  The heavy isotope of hydrogen, which contains a neutron as well as a proton in the nucleus of the atom. The dilution of a sample of deuterated water (D₂O) in the body fluids can be used as a measure of total body water.

**disinhibited eating**  A period of out-of-control or excessive eating within the context of intentionally controlled or restricted eating for the sake of weight loss or weight control.

**disinhibition**  Uncontrolled eating or other action in response to cognitive or emotional cues.

**dizygotic**  Resulting from fertilization of two eggs, which results in non-identical (fraternal) twins, as opposed to monozygotic (identical) twins.

**dopamine**  A catecholamine that is a neurotransmitter and precursor of epinephrine and norepinephrine; it is synthesized from tyrosine.

**dopaminergic system**  Related to dopamine, a neurotransmitter, such as a synapse that uses dopamine or a receptor that responds to it.

**double-blind**  The condition in an experimental study where neither the researcher nor the participant knows whether the subject is assigned to the experimental or control group. This design is used to reduce the effects of bias and suggestion on study outcomes.

**doubly labeled water**  A method used to estimate energy expenditure in the free-living individual. The person drinks a known sample of water that has been enriched with water containing stable isotopes of oxygen (O¹⁶) and deuterium (H²). The rate of disappearance of the labeled water from the body water, usually over the course of about 2 weeks, can be used to estimate the person’s energy expenditure during that period.
**dual-energy X-ray absorptiometry (DEXA, DXA)**  A method for measuring the density of bone mineral, using two x-ray beams of different energies. Because the method distinguishes the differential attenuation of the two beams by bone and lean and fat soft tissue, it enables estimation of bone, lean, and fat content.

**dumping syndrome**  Condition where there is rapid gastric emptying and undigested stomach contents are “dumped” into the small intestine. Symptoms include abdominal cramps, diarrhea, flushing, and sweating, which may occur after stomach surgery, especially if simple sugars are ingested.

**duodenoileostomy**  A surgical procedure that connects the ileum to the duodenum.

**ecological fallacy**  The false inference that what is true for group data is true for the individuals that contributed to the group data.

**ecological model**  A model that considers multilevel influences on behavior, including individual, relationship, community and broader societal characteristics.

**afferent signals**  Signals sent away from the site of their origin. With respect to the central nervous system, many afferent neural fibers carry signals to other parts of the body.

**endocannabinoid**  A set of receptors, found in many tissues throughout the body, and their activating lipids (including those in cannabis/marijuana). This system is involved in a variety of processes including memory, appetite, pain, blood pressure regulation, etc.

**endometrium**  The lining of the uterus.

**endothelin**  A peptide made by the vascular endothelium, with synthesis and release stimulated by shearing physical forces and by numerous circulating compounds including antidiuretic hormone, cytokines, angiotensin II, thrombin, etc.

**epigenetic**  Effects resulting from differences in gene expression levels rather than from different gene/DNA sequences. Some of these effects result from alterations in the genome due to methylation of DNA or acetylation of histones.

**evidence-based treatment guidelines**  Guidelines developed from systematically reviewed scientific evidence.

**exercise intrinsic motivation**  An individual’s level of motivation for exercise with regard to enjoying and being interested in exercise.

**exercise self-efficacy**  The extent to which a person believes that he or she can stick with an exercise program under varying circumstances (e.g., when lacking time, when feeling tired).

**eye-safe class-1 laser-light**  A laser light that is classified as safe for the eyes under all conditions of normal use.

**fascia**  A layer of fibrous tissue that acts to divide or bind together different portions of organs, muscles and various soft parts of the body.

**femoral-gluteal area**  The area including the thigh and buttocks.

**fen-phen**  A pharmaceutical used for weight loss and made up of fenfluramine and dexfenfluramine. It was withdrawn from the market in 1997 because of an observed high frequency of abnormal echocardiograms in users.

**First Nation**  Organized aboriginal groups of Canada, especially those with official government recognition. It does not include the Inuit or Métis peoples.

**flexible cognitive restraining**  A lack of emotional and disinhibited eating, characterized by a more graduated approach to eating and weight control (as opposed to rigid cognitive restraint, which is characterized by a dichotomous approach).

**food frequency questionnaire**  A dietary assessment method in which subjects select from several offered alternative foods or food groups the frequency of consumption and (usually) the portion size eaten.

**Framework Convention on Tobacco Control (FCTC)**  A treaty coordinated by the World Health Organization; it attempts to minimize the adverse effects of tobacco worldwide. In 2004, it had more than 168 signatories. It is among the most widely supported treaties in the history of the United Nations.

**functional analysis**  The examination of antecedent events and consequences of problem behaviors.

**functional foods**  Foods that have a special ingredient or ingredients added with the purpose of promoting the food for disease prevention or health promotion. Meal replacements may be considered functional foods if they are fortified with vitamins, minerals, fiber or other food components that are purportedly “functional” in the sense that they are intended to support weight loss.

**gastric bypass**  Surgical procedures designed to cause food to bypass most of the stomach.
gastroesophageal reflux The movement of stomach contents and acid upward into the esophagus. It causes heartburn and can damage the cells lining the esophagus.

genome-wide linkage scan A method used to study the extent to which a given trait (or phenotype) is associated with a specific gene or genes.

genomic imprinting Pattern of inheritance in which the expression of a nuclear gene is based on whether an individual inherits the gene from the mother or father.

ghrelin A hormone, made in the lining of the stomach fundus, which is the only currently known peripheral hormone that increases appetite (orexigenic).

GLP-1 Glucagon-like peptide, a gut peptide, released from the intestine following a meal, shown to inhibit feeding.

HAM-D depression scales (Hamilton Rating Scale for Depression) A scale to be administered by a health professional and used to classify the severity of depression in a subject diagnosed as having a depressive disorder.

Harris-Benedict equation An equation that estimates total daily energy expenditure by applying an activity factor to the estimated basal metabolic rate.

health belief model A model for predicting and explaining a person's health behavior, based on his or her attitudes and beliefs, such as perceived susceptibility and severity of the health condition and benefits of and barriers to its treatment.

health risk appraisal (HRA) A 62-question self-administered form that covers behaviors and lifestyle conditions that influence or reflect health risk.

hepatic steatosis The build-up of excessive amounts of fat in liver cells.

heritability The extent to which genetic differences among individuals contribute to differences in observed characteristics of those individuals.

heritability estimation A method for determining the genetic contribution to a trait of interest. Data are obtained from close relatives of the index case, such as siblings, parents, and offspring, and a statistical method is used to determine the inheritance pattern among the relatives.

higher cortical functions Functions of the brain involving thinking and knowing, including such processes as language, memory, concentration, etc.

hydodensitometry Determination of the weight of a body when it is under water. Used with Archimedes principle to determine the density of the human body, from which body fat percentage can be estimated.

hypothalamic-pituitary-gonadal (HPG) axis The combined effects of these three endocrine glands, which often operate in concert in the development and regulation of a wide array of body systems involved in reproduction and growth.

hypothalamic-pituitary-thyroid An interacting group of glands that regulate metabolism by way of a feed-back loop dependent on the release of thyrotropin releasing hormone (TRH) from the hypothalamus, the release of thyroid stimulating hormone (TSH) from the pituitary, and the release of thyroxine from the thyroid gland.

hypothalamus A part of the brain involved in the production of several hormones that are important in a wide array of body functions, including body temperature regulation, lactation, food intake, water balance, etc.

IGF-1, Insulin-like Growth Factor-1 A peptide, produced by the liver, which stimulates growth processes.

impedance The tendency of matter to resist the flow of an electric current. It is measured during BIA (bioelectric impedance analysis), a method used to estimate body water.

Implicit Association Test (IAT) A standardized test designed to measure a person’s implicit beliefs and attitudes about an array of issues, such as race, body weight, sexual orientation, political figures, etc., to reveal attitudes and beliefs that the person otherwise is unable or unwilling to report.

indirect calorimetry An approach to determine energy expenditure by measuring a person’s oxygen consumption, carbon dioxide production, and minute ventilations (the amount of air a subject breathes in one minute).

innate immune response Immunity present from birth and not dependent on prior antigen exposure. Innate immunity includes physical and chemical barriers to infection, such as phagocytes, complement, and natural killer cells.

Institute of Medicine A not-for-profit organization, part of the National Academy of Sciences. It has as its mission, “to serve as adviser to the nation to improve health. The Institute provides unbiased, evidence-based, and authoritative information and advice concerning health and science policy to policy-makers, professionals, leaders in every sector of society, and the public at large” (www.iom.edu/CMS/AboutIOM.aspx).
intertriginous rashes A rash that develops on opposing surfaces of folds in the skin (e.g., the armpit, neck, fat folds, and under pendulous breasts), due to the warmth, friction, and moisture at these locations.

knock-in mice A mouse that has been genetically altered by having specific genetic information inserted into its DNA.

knockout mice A genetically altered mouse in which a specific gene or genes have been rendered inactive to enable study of their function.

leg-to-leg pressure contact BIA A bioelectrical impedance body composition measurement method, where the electrode contact is made through the feet by standing on pressure-contact electrodes on a scale, rather than using arm and leg gel-contact electrodes.

leptin A polypeptide hormone produced by adipose tissue. It has an important role in the regulation of energy balance, acting on the hypothalamus to suppress appetite.

leptin resistance A condition where the response to a given blood level of leptin is blunted.

linkage analysis A statistical method for determining the tendency for genes (and their functions) to be inherited together, based on their proximity on the chromosome.

lipodystrophy/lipoatrophy A syndrome characterized by impairment or abnormality in adipose tissue accumulation.

lipostatic Involved in the maintenance of body fat stores.

lipotoxicity Adverse health effects resulting from the excessive accumulation of fatty acid in non-adipose tissues.

locus of control A person’s belief about the determinants of the events in his or her life, that is, whether they are determined externally or by the person’s own actions.

Master Settlement Agreement (MSA) An agreement signed by officials of 46 US states and several US territories and the five largest tobacco companies, to resolve and settle the states’ law suits against the tobacco companies, and to alter the marketing methods used to target youth. Under the agreement, the states would receive a settlement of $206 billion over a period of 25 years. The anti-smoking Legacy Foundation was established as a result of this agreement.

MC4R antagonist A compound that antagonizes the function of the melanocortin-4 receptor (MC4R) in the brain, potentially increasing food intake and causing obesity.

MCH knockout mice A mouse that has been altered genetically so that it does not have normal function of its melanocyte concentrating hormone (MCH). It thus eats less and remains lean.

MCH receptor-null A genetic alteration that inactivates the receptor for melanocyte concentrating hormone (MCH) so that it does not have normal function. Affected animals eat less and remain lean.

mean absolute intra-pair difference The mean absolute difference in the values of a variable obtained from twin pairs.

measured genotype approach An approach to identifying the multiple genes that influence traits, such as blood pressure, that can vary in a continuous manner.

mesodermal Relating to the mesoderm, an embryonic tissue that is the precursor to muscle, connective tissue, the skeleton, and many of the internal organs.

mesolimbic pathways A neural dopamine pathway in the brain, which connects the midbrain to the prefrontal cortex, and functions in the reward system of the brain.

metabolic syndrome A constellation of factors associated with increased risk for atherosclerotic cardiovascular disease, type 2 diabetes, and their complications. This constellation consists of metabolic risk factors, atherogenic dyslipidemia, elevated blood pressure, elevated blood glucose, a prothrombic state, and a proinflammatory state. Originally called Syndrome X.

missense mutation A mutation in a protein-coding gene that causes the substitution of one amino acid for another in the protein produced.

monoamine oxidase inhibitor A compound or medication that blocks monoamine oxidase, an enzyme that inactivates some neurotransmitters.

monozygotic In twinning, resulting from the fertilization of one ovum, producing genetically identical offspring.

motivational interviewing A counseling style that aims at inducing behavior change through directed exploration and resolution of a client’s ambivalence.

myeloid progenitor cells Cells from the bone marrow that give rise to circulating monocytes.

National Health and Nutrition Examination Survey An ongoing survey research program implemented by
the National Center for Health Statistics (NCHS) of the Centers for Disease Control and Prevention (CDC) of the US Department of Health and Human Services to monitor the nutritional and health status of US adults and children, using interviews, laboratory tests, and physical examinations.

natural experiment An “experiment” made possible because of a changed condition that was not brought about by the researchers, but was a natural consequence of some notable event, such as war, famine, flooding, etc.

neuroimaging Any method used to image the structure or function of the brain.

neuromedin B A peptide found in the CNS and GI tract, the human analogue of bombesin; it inhibits feeding.

neurotrophic Having an effect on the growth, differentiation, migration, survival, interactions, and proliferation of neuronal and glial cells of the brain. Neurotrophic factors are involved in determining many complex behaviors such as feeding, learning, and mood.

non-exercise activity thermogenesis (NEAT) The heat generated by the body due to low-level physical activities not usually classified as exercise (e.g., fidgeting, position-shifting, etc.).

non-resting energy expenditure The energy expenditure of a person under conditions of ordinary daily activity.

noradrenergic Involving norepinephrine in a process, such as transmitting nervous impulses.

odds ratio (OR) Ratio of the odds of disease among an exposed group compared with the odds of disease among an unexposed group. For rare diseases, the odds ratio is an estimate of the relative risk.

operant conditioning A learning principle in which consequences, such as reward and punishment, influence the likelihood of a behavior being repeated.

opioid system A set of receptors and their activating compounds, which include enkephalins and endorphin released by neurons, and exogenous compounds such as opiates (morphine, heroin). This system is involved in reward, pain, and addiction.

paracrine A method of communication between cells whereby a chemical signal is released by one cell into the extracellular space, where it acts locally on neighboring cells.

parasympathetic nervous system The subdivision of the autonomic nervous system that dominates in quiet, relaxed situations and promotes body maintenance activities such as digestion and emptying of the urinary bladder.

parvicellular region A part of the paraventricular nucleus of the hypothalamus, characterized by small to medium-sized neurons. The area is concentrated with neurons secreting thyroid-releasing hormone and also contains neurons secreting corticotrophin-releasing hormone, enkephalin, galanin, and other compounds.

PAT domain A region of a protein with an amino acid sequence that is similar to a sequence found in the PAT family proteins, perilipin, ADRP, and TIP47.

peptide YY3-36 (PYY3-36) A 36-amino acid peptide that inhibits feeding. It is released by the gastrointestinal tract in response to feeding.

PET studies Positron emission tomography, an imaging method that uses positron emitting substances to produce three-dimensional images of the body. When 18F-labeled 2-deoxy-2-fluoro-D-glucose (18F-FDG) is used as a tracer, the images indicate the extent of glucose metabolism in various locations.

phenocopy An organism that manifests traits that resemble the traits produced by a different genotype. The traits are caused by unusual environmental conditions rather than the organism’s genotype.

phenothiazines A group of compounds with a similar structure, some of which are tranquilizers, such as chlorpromazine.

phenotype The external manifestation of physical or other visible characteristics that are the result of genes and their interactions with environmental factors.

phenotypic variance The variations seen in a given phenotype.

phenotypic Relating to the observable characteristics of an organism.

phosphoinositol-3 kinase (PI3K) A group of enzymes sharing the ability to phosphorylate phosphatidylinositol. They play a role in the regulation of glucose uptake.

plasminogen activator inhibitor (PAI)-1 An inhibitor of tissue plasminogen activator, produced in several tissues including the endothelium and adipose tissue. It inhibits fibrinolysis and thus supports clotting.

PNS tone The level of activity of the parasympathetic nervous system on a chronic basis.

dyg cystic ovary syndrome A hormonal disorder associated with irregular ovulation, hyperandrogenism,
and infertility. Insulin resistance, obesity, and diabetes rates are higher in women with this condition.

**POMC, pro-opiomelanocortin** A polypeptide synthesized in the pituitary, which when cleaved produces many peptides with a diversity of cellular functions, including adrenocorticotropic hormone, melanotrophins, and endorphins.

**Prader-Willi syndrome** A genetic disorder with manifestations including obesity, mental retardation, and low muscle tone.

**pre-adipocyte** A mesodermal fibroblast-like cell present in adipose tissue. It can differentiate into a mature adipocyte.

**progestational hormones** Steroid hormones important for the maintenance of pregnancy, such as progesterone.

**prohormone** A precursor to a hormone; it generally has little intrinsic hormonal activity.

**prolactin** A peptide hormone produced by the anterior pituitary, important for breast development and milk secretion.

**pro-thyroid releasing hormone** A hormone, originating in the hypothalamus, which is a precursor of thyroid releasing hormone, a tripeptide that is required for normal thyroid function; it stimulates the release of thyroid-stimulating hormone and prolactin by the anterior pituitary.

**pseudotumor cerebri** A condition involving elevated intracranial pressure of unknown cause, mostly affecting obese women of childbearing age; it can result in blindness.

**psychoeducation** Information regarding psychological principles that guide human behavior. During psychoeducation, the patient is provided with knowledge about the condition, the causes of the condition, and the reasons why a particular treatment might be effective for reducing the symptom.

**PYY₃₋₃₆** See peptide YY.

**quantitative trait locus (QTL) studies** A research strategy used to identify a DNA region or genes that determine disease susceptibility.

**quasi-experiments** A study design that does not involve random assignment.

**RE-AIM approach:** RE-AIM is an acronym that consists of five elements, or dimensions, that relate to health behavior interventions: Reach the target population; Efficacy or effectiveness; Adoption by target settings or institutions; Implementation—consistency of delivery of intervention; Maintenance of intervention effects in individuals and populations over time (www.re-aim.org/2003/FAQs_basic.html).

**renin-angiotensin-aldosterone system (RAAS)** A set of hormones that act together to regulate blood pressure.

**resistin** A hormone named for its role in “resistance to insulin.” It is thought to contribute to the link between obesity and type 2 diabetes.

**resting metabolic rate (RMR)** The rate at which the body burns calories while at rest under thermoneutral (neither hot nor cold) conditions and in a post-absorptive state (at least 8 hours since the end of the last meal). RMR is proportional to lean body mass, so if a significant amount of lean body mass is lost during weight loss, RMR declines.

**RNA interference (RNAi)** A laboratory method for preventing the actions of a gene after it has been transcribed; it operates through a single-strand RNA that is complementary to a section of the mRNA of the gene.

**serotonergic** Related to serotonin, such as a neuron that uses serotonin or a receptor that responds to it.

**serotonin** A neurotransmitter synthesized in the brain and found in many tissues and in the serum. It is a vasoconstrictor and reduces gastric secretion.

**single blind** A study design in which subjects do not know whether they have been assigned to an experimental or control (often placebo) group, while the researchers can have that knowledge.

**sleep apnea** A condition in which breathing ceases repeatedly during sleep, for longer than normal periods.

**social capital** Connections within and between social networks and among individuals, thought to have value and to affect the productivity of individuals and groups.

**social marketing** The use of commercial marketing methods for the purpose of changing behavior to achieve a social benefit.

**sulfonylureas** A group of pharmaceuticals taken orally. They stimulate secretion of insulin by the pancreas.

**summative evaluation** Evaluative methods intended to assess whether an intervention, usually an educational one, was effective as implemented. It is contrasted to formative evaluation, which is an evaluation of whether the intervention was applied as intended.
surgical vagotomy  Surgical cutting of the vagus nerve. Reduces production of stomach acid.

sympathetic nervous system  A part of the autonomic nervous system activated in situations involving stress, intense physical activity, danger, etc.

sympathomimetic  Mimicking the effects of the sympathetic nervous system.

thermic effect of food  The energy used to process, digest, absorb, and store ingested nutrients.

thiazide  A group of drugs used in the treatment of hypertension. They block sodium resorption in the kidney.

thiazolidinediones  A class of drugs, also called glitazones (including rosiglitazone, pioglitazone and rosiglitazone), used to lower insulin resistance in type 2 diabetes.

total and direct bilirubin  A blood test that measures conjugated and unconjugated bilirubin, a product of the metabolism of the heme moiety of hemoglobin. Blood levels are used to screen for problems of the liver or gall bladder.

tumor necrosis factor α (TNF α)  A proinflammatory cytokine, also called cachexin, involved in the acute phase response. It regulates immune cells, can cause cell death, and inhibits tumorigenesis and the replication of viruses.

ventral tegmental area  An area at the center of the brain, which integrates information from other regions about the status of vital functions; it then sends dopamine signals to other brain regions, reinforcing behaviors essential for survival.

waiting list control group  Subjects willing to be in a treatment group but placed on a waiting list and later used as a control/comparison group. They are likely to be more similar to the experimental group than an untreated comparison group chosen differently.

Wernicke’s syndrome  A disease manifested by confusion, hypothermia, hypotension, coma, and other signs, due to degeneration of the brain caused by a lack of thiamin.

whole body ergometry  The measurement of work done by the body.

X/A-like cells of the stomach mucosa  Neuroendocrine cells of the fundus of the rodent stomach; they synthesize and secrete ghrelin into the blood. P/D1 cells are the analogue in humans.
Introduction

As the writing of this textbook was concluding in 2010, The Strategic Plan for NIH Obesity Research was released for public comment. The research plan starts with a simple description of obesity resulting from a mismatch in energy balance, whereby calories taken in from food and beverages exceed those expended in activity and metabolic functions to result in excessive adipose tissue (body fat) storage. From this straightforward beginning, the plan goes on to describe the many ways in which the growing prevalence of obesity is a highly complex phenomenon, requiring multifaceted research in a wide variety of disciplines. Obesity research is conducted at a number of levels, focusing on molecules, cells, tissues, organs, systems, and behaviors throughout the lifecycle at the individual level as well as the interplay of factors and dynamics that prevail in families and communities which are influenced by social, economic, and political realities prevailing in the United States in the 21st century and in developed and developing countries around the globe.

Reflecting that complexity, this book is presented to the reader in 27 chapters, organized into five parts. The first four chapters, constituting Part I, help the reader understand the scope and complexity of the problem of obesity. Part II focuses on obesity etiology—a topic so complex it requires six chapters, ranging from a discussion of genetic and other biological contributions to physiological and environmental factors that are thought to be causal. Part III examines the health consequences of obesity for both children and adults. Part IV discusses the challenge of assessing obesity in humans and offers insights into community factors that influence the risk of obesity. Finally, Part V dedicates 13 chapters to a discussion of a wide variety of prevention and obesity treatment interventions currently in use. The authors of each chapter were asked to identify questions that future research might answer.

What we have also strived to capture is the sheer excitement of discovery that drove generations of researchers to make their contributions to our current understanding of obesity. That understanding has grown, piece by piece. But progress is not always incremental. Below we have chosen to describe one example of a revolution in our understanding of obesity. This illustrates not only the excitement of discovery, but also the serendipity that sometimes permits several lines of scientific inquiry to converge into a momentous leap forward. This example informs the way some researchers now think about the interface between genetics and environment—that genetics loads the gun, but environment pulls the trigger.

The excitement of discovery

In the 1950s, workers at the Jackson Laboratory in Bar Harbor, ME developed a genetically obese mouse—the $ob/ob$ mouse—which became the focus of innovative research conducted by Douglas Coleman in the 1960s. Mice that carry two copies of the $ob$ or obesity trait are obese but infertile. Consequently, the development of a sizeable population of these animals required for research purposes involved the painstaking mating of lean animals.
Only two years later, a case of human genetic obesity due to leptin deficiency was identified in a Pakistani child who exhibited extreme and marked obesity at an early age. That this child’s disease could be corrected by exogenous administration of leptin illustrates how several avenues of research conducted by academic, clinical, and industry researchers converged to permit positive identification of this rare form of genetic obesity. This clinical case was the first to provide indisputable evidence illustrating that human obesity can result from a genetic defect that caused marked hyperphagia and excess fat deposition. This launched the race to identify the mechanisms by which this sequence of events occurred and has profoundly influenced thinking about how genes and the environment interact to promote expression of the obese phenotype. Many sensed that the field of obesity was changed forever, attracting an influx of researchers from a variety of disciplines such as neuroscience and cell biology seeking to untangle the web of overlapping systems regulating food intake, energy expenditure, and ultimately, energy balance.

As important as the discovery about the genetic bases of obesity are, there is also a recognition that energy balance is a confluence of many complex gene–environment interactions, Some of which are set in motion in utero. These complex interactions are highlighted in many chapters and it is our hope that as readers learn about the epidemiology or prevalence of obesity, the health consequences and prevention or treatment of obesity, they will be introduced to many of the unanswered questions that challenge us today. If those reading find that their imagination fired and curiosity is piqued, then we will have achieved what we set out to do.
Part I
Understanding the Scope

Introduction

Part I, Understanding the Scope, covers broad topics and includes the epidemiology, etiology, and consequences of obesity, as well as its cultural and psychodynamic perspectives. Currently, worldwide, there are about 1 billion overweight people, 300,000 of whom are obese, and more than two-thirds of the US population are now overweight or obese. Since obesity contributes to several chronic diseases, it has become a major public health problem. This first part will also consider what can be learned from other public health initiatives (e.g., smoking) to stem the tide of overweight and obesity.

Chapter 1, Epidemiology, Etiology, and Consequences of Obesity, an overview for the entire book, presents current definitions of obesity, epidemiological data on the growing prevalence of obesity and its consequences, and some of its putative causes. The chapter systematically explains the definition of overweight and obesity and the contribution of the amount and distribution of body fat to the development of type 2 diabetes, heart disease, and other chronic diseases related to obesity. A review of etiological factors reveals that many factors combine to create positive energy balance. Hence, it is difficult to measure the contribution of any one factor.

Chapter 2, Cultural Attitudes and Biases Toward the Obese, addresses the pervasive existence of weight bias in western cultures. This bias is harmful to children and adults; for the rates of weight bias are similar to or higher than other forms of discrimination, such as racial discrimination. The consequences of weight bias can be severe and enduring; they include impaired mood, low self-esteem, and, in some cases, suicidal ideation. Though high to begin with, the rates of weight bias are increasing, and the chapter emphasizes the need for research to understand and reverse the trend.

Chapter 3, The Application of Public Health Lessons to Stemming the Obesity Epidemic, places obesity in the context of other major public health challenges. The goal of this chapter is to focus on successes achieved in these other spheres, including tobacco control, injury prevention, and underage alcohol use, and to apply the lessons learned to obesity prevention models. The chapter reviews models of health behavior and planning that diagnose problems, identify contributing factors, and develop interventions to solve the problem. Obesity prevention, especially childhood obesity prevention, views the individual in the larger context of the family, community, and society. This “ecologic framework” has proven utility in other public health interventions and will likely have utility in obesity prevention. The approach will lead to interventions that balance targeted approaches to individuals, and emphasis on changing the broader environment in which they live.

Chapter 4, Psychodynamic Approaches to the Treatment of Obesity, addresses the psychological impact of obesity in US society. Building on the phenomena described in Chapter 2, this chapter focuses on the impact of the puritanical roots in US society and the idea that with sufficient effort and focus, anything, including thinness, is achievable. With this framework, obesity is seen as a moral failure. Perhaps even more striking is the fact that obese people perceive themselves as a failure; this can begin in childhood and persist into adulthood.
The chapter focuses on the psychological meaning of food, appetite, and weight. In addition, the psychological consequences of recidivism and weight regain are addressed.

Collectively, these four chapters set the stage for understanding the global trends in obesity, and its etiological, cultural, and psychological factors. It also creates a framework for thinking about how the obesity epidemic is both similar to, yet different from, other major public health challenges.
Epidemiology, etiology, and consequences of obesity

Barbara J. Moore and Xavier Pi-Sunyer

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 (kg/m²). 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>
<thead>
<tr>
<th>Classification</th>
<th>BMI (kg/m²)</th>
<th>Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Underweight</td>
<td>&lt;18.5</td>
<td>Increased</td>
</tr>
<tr>
<td>Normal</td>
<td>18.5–24.9</td>
<td>Normal</td>
</tr>
<tr>
<td>Overweight</td>
<td>25.0–29.9</td>
<td>Increased</td>
</tr>
<tr>
<td>Obese Class I</td>
<td>30.0–34.9</td>
<td>High</td>
</tr>
<tr>
<td>Obese Class II</td>
<td>35.0–39.9</td>
<td>Very high</td>
</tr>
<tr>
<td>Obese Class III</td>
<td>≥40</td>
<td>Extremely high</td>
</tr>
</tbody>
</table>

Table 1-1 BMI-associated disease risk

The use of body mass index (BMI) has been proposed by the National Institutes of Health, a the Centers for Disease Control and Prevention, b and the World Health Organization c 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 kg/m², and increases further at a BMI of 30 kg/m². 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.

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