Chronic Disease Prevention

CHAPTER OUTLINE

I. OVERVIEW OF CHRONIC DISEASE

Whereas infectious diseases were long a major determinant of both quality and length of human life, and remain so in much of the developing world, the burden of morbidity and premature mortality in developed countries shifted dramatically over the 20th century to so-called chronic diseases. The term "chronic disease" is less useful than in the past because even infectious diseases such as human immunodeficiency virus (HIV) have become "chronic" with the advent of effective treatments in the absence of cure. In essence, any disease that can be effectively managed over years or decades, but not cured, is chronic. The term *chronic disease* is applied preferentially, however, to conditions described as follows:

- Not directly transmissible person to person
- Routinely span years and often decades
- Degenerative in some way, relating to aberrant or declining function of some body part or system
- Often propagated by fundamental physiologic imbalances or disturbances, such as inflammation

The conditions of greatest concern—contributing most to years lost from life, life lost from years, and costs—are cardiovascular diseases (including stroke), cancer, pulmonary diseases, and diabetes and related metabolic derangements. These conditions now constitute the leading causes of mortality worldwide. In addition, conditions such as osteoarthritis, chronic pain syndromes, and depression exact a high toll in morbidity and cost, generally without imposing a direct mortality toll.

Of particular interest to epidemiologists is the strong body of evidence suggesting that fully 80% of chronic disease is potentially preventable by means already available, and that even genetic risk factors for chronic disease development and progression are modifiable by the effective application of lifestyle interventions.

A. The Human Toll

A short list of chronic diseases—heart disease, cancer, stroke, diabetes, and chronic lung disease—constitute the leading force of worldwide mortality. More than 60% of all deaths in the world each year are attributable to this short list of conditions.[1]

In some ways, the mortality toll of chronic diseases can exaggerate their harms. Chronic degeneration of vitality and function is, to one degree or another, the human fate until such time as the "rectangularization" of the mortality curve can be converted from an aspiration to prevailing reality[2] (Fig. 19-1). As life expectancy rises, so does the opportunity for time-dependent degeneration of organ systems. Chronic, degenerative disease is simply a point along this spectrum and thus inescapable under prevailing conditions if persons live long enough; we must eventually die of something. To the extent chronic disease merely represents this inevitable "something," the attributed death toll can make the situation seem worse than the reality. Not succumbing to infectious or traumatic causes of death early in life partly makes us vulnerable to chronic diseases later. The importance of causes of death earlier in life is best captured not by the number of deaths but by the number of *years of potential life lost* (see Chapter 24).

In another important way, however, the mortality toll of chronic diseases greatly underestimates the human cost. Long before taking years from life by causing premature death, chronic diseases take *life from years* by reducing ability, function, vitality, and quality. This is an ever more salient concern because chronic diseases, driven largely by a short list of lifestyle factors and particularly their relationship to obesity,[3] occur at ever younger ages. What was called only a generation ago "adult-onset diabetes" is now called type 2 diabetes and routinely diagnosed in children. The proliferation of cardiac risk factors in ever younger children is well

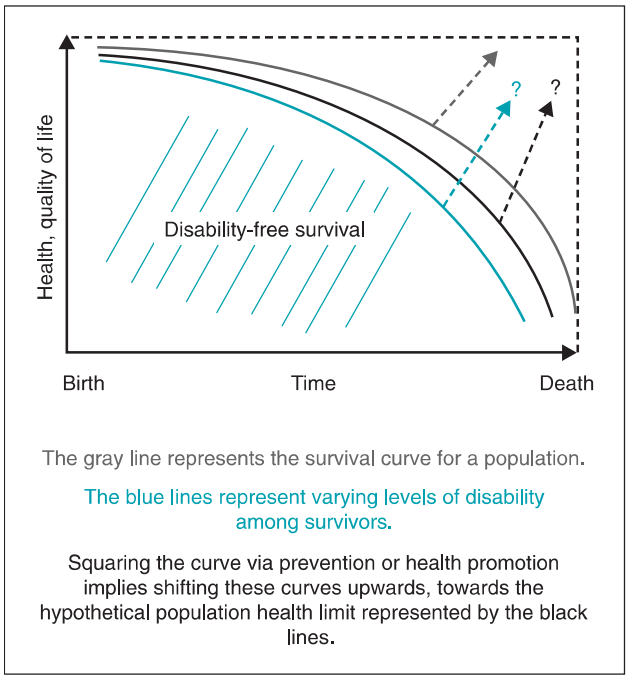

Figure 19-1 The concept of rectangularizing, or squaring, the survival curve. (From *Society, the individual, and medicine*, Ottawa, Canada, 2010, University of Ottawa. www.med.uottawa.ca/sim/data/Rectangularization_of_mortality_e.htm)

documented.[4] Further, the occasional lifestyle-related cancer is diagnosed in surprisingly younger persons. A marked increase in the rate of stroke among children age 5 to 14 years also has been reported.[5]

Collectively, these trends indicate the importance of factoring the chronicity of chronic disease into any assessment of the human cost. As serious and potentially disabling disease begins at ever-younger ages, mortality becomes an increasingly less useful measure of the total impact of these conditions. A measure of attenuated quality of life, adjusted for the life span affected, is most suitable[6] (See Chapters 14 and 24 for quality-adjusted life years [QALY] and disability-adjusted life years [DALY]). By such a metric, the human cost of chronic disease is enormous, and it continues to rise.

B. The Financial Toll

There are glib expressions in the halls of medicine about the relative financial costs of life and death. Death is, in financial terms, inexpensive as expenditures related to treatment and preservation of life cease. Life, burdened by chronic disease, can be enormously expensive. As we grow ever more adept at forestalling death through the application of pharmacotherapy, procedures, and medical technology, the costs of living with chronic disease are rising. In the United States, more than 75% of Medicare expenditure (hundreds of billions of dollars annually) is for chronic disease.[7]

As with the mortality statistics, these costs represent several mixed messages. The positive message is that costs of chronic disease care rise as this care becomes more effective. When treatments are ineffective, death comes earlier. More effective treatment is unquestionably good, but means a longer treatment period before death and thus higher costs. Advances in pharmacotherapy and technology tend to improve treatment and function (favorable) but generally involve higher costs (unfavorable). The positive message lost in gloomy statistics about cost is that we are "getting what we are paying for": longer lives despite the high and rising prevalence of chronic disease.

Other messages related to the financial costs of chronic disease are decidedly less positive. As addressed later, chronic diseases are substantially preventable by means already available. The reliance on high-cost treatment is to some degree testimony to the failure to make better use of lower-cost prevention. There is also widespread failure to treat risk factors such as high blood pressure and dyslipidemia to target levels.[8,9]

Also, the *direct* financial costs of chronic disease care do not fully capture the economic toll. Reduced productivity, absenteeism, presenteeism (attending work while sick), and related effects, known in economic terms as *externalities* or *indirect costs* (or benefits; externalities can be positive as well as negative), are high and may even exceed the direct costs.[10]

Projections about the financial costs of chronic disease are genuinely alarming and constitute nothing less than a crisis, questioning the fundamental solvency and economic viability of the U.S. health care system beyond the middle of the 21st century should current trends persist. As a result, there is increasing awareness about the importance of chronic disease prevention and the strategies that will convert what is known in this area into what is done, as well as increased attention to better management of chronic disease with patient-centered medical homes[11] and the chronic care model.[12] Professionals directly involved in public health and preventive medicine have a clear opportunity to advance the mission of prevention in responding to the dangers of the chronic disease crisis.

C. Common Elements in Pathogenesis

There is increasing appreciation for a unifying constellation of processes that underlie most if not all chronic degenerative diseases.[13,14] These pathways and their details will spawn discussion and debate for years. A case may be made, however, for a short list of common pathways, as shown in Box 19-1.

Of particular relevance in the context of epidemiology is that a common constellation of factors underlying most or all chronic diseases suggests the presence of common pathways to prevention as well. This indeed appears to be the case; the same short list of lifestyle factors appears to influence the likelihood of all major chronic diseases across the life span, other factors being equal (see Box 19-2). The notion of common pathways to diverse morbidities has been embraced by leading health agencies[15] and the National Institutes of Health (NIH).[16]

II. PREVENTABILITY OF CHRONIC DISEASE

Literature spanning at least the past two decades makes a compelling case that the leading causes of premature death—and thus the leading causes of chronic morbidity, because they are the same—are overwhelmingly preventable by means already available. A seminal 1993 paper first highlighted that chronic diseases leading to premature death were not meaningfully "causes" of death but rather "effects."[17]

Box 19-1 Four Pathophysiologic Pathways in Chronic Disease*

1. Cellular Senescence

Aging, or *senescence,* at the organ system and cellular levels encompasses gradual attenuation of function (e.g., age-related decline in glomerular filtration rate) and ultimately a termination of cellular renewal and the loss of formerly functional cells through *apoptosis* (programmed cell death). Chronologic and biologic aging are related but different. *Chronologic aging* refers to a measure in units of actual time; *biologic aging* refers to function relative to age-standardized norms. By either measure, the time-dependent attenuation of functional capacity is a common element in the development and progression of chronic diseases.

2. Degeneration

Degeneration can occur as a time-dependent process but can also occur independently. Cumulative injury to the vascular lining caused by hypertension is an example of degeneration, as is the erosion of articular cartilage caused by "wear and tear" that leads to osteoarthritis.

3. Oxidation

A preoccupation with the health-promoting potential of antioxidants derives from the harmful potential of oxygen free radicals generated both in defense of the body against pathogens and as a byproduct of metabolic activity. Oxidation is implicated as a facilitator of virtually all chronic diseases.

4. Inflammation

Inflammation is a generic term referring to a range of immune system actions, both in response to and independent of infection. The action of various white blood cell lines, cytokines, immunoglobulins, and complement can defend the body against pathogens but can also cause damage to native tissue and healthy cells. Dietary imbalances, with resultant hormonal imbalances, related in particular to eicosanoids (prostaglandins), cortisol, and insulin, are implicated in chronic inflammation, which in turn is implicated in the propagation of most chronic disease.

*Common to most if not all chronic diseases. These processes provide important insights about the potential to prevent chronic disease, as well as opportunities to prevent multiple chronic diseases by addressing a common cluster of causes.

Box 19-2 Ten Controllable Factors in Prevention of Chronic Disease

Tobacco	Toxic agents
Diet	Firearms
Activity patterns	Sexual behavior
Alcohol	Motor vehicles
Microbial agents	Drug use

Modified from McGinnis JM, Foege WH: *JAMA* 270:2207–2212, 1993.

These effects—the chronic diseases—were the result of 10 factors, mostly behaviors that individuals can control (Box 19-2). Using the epidemiology of 1990, this analysis found that about 80% of all premature deaths were attributable to the first three entries: tobacco, diet, and activity patterns (physical activity). Alliteratively, the leading causes of chronic disease and premature death in 1990 were "how we used our feet, our forks, and our fingers."

In 2004 the U.S. Centers for Disease Control and Prevention (CDC) updated and supported the same fundamental conclusions.[18] The same is true of subsequent related studies.[19-21] In addition, recent and accumulating evidence indicates that lifestyle interventions can modify gene expression and thus alter the risk for chronic disease development and progression at the genetic level.[22,23] In the aggregate, this literature belies the importance of the nature/nurture debate by highlighting the hegemony of "epigenetics" and the apparent human potential to "nurture nature."

The available data from diverse sources suggest that about 80% of all chronic disease could be prevented. With regard to specific conditions, 80% or more of cardiovascular disease; 90% or more of diabetes; and as much as 60% of cancer are thought to be preventable with the use of resources already available. Were this knowledge to be translated into the power of routine action, it would increase life expectancy and add much more to health expectancy, or the "health span."[24] In blunt terms, if and when we find the means to turn what we know about the prevention of chronic disease into what we routinely do, it would constitute one of the most stunning advances in the history of public health (see Chapter 28).

III. CONDITION-SPECIFIC PREVENTION

A. Obesity

There is debate about the appropriateness of classifying obesity as a chronic disease. Obesity is clearly established as a risk factor for virtually all major chronic diseases. Whether obesity itself qualifies as a disease is important in several ways. First, obesity bias is a prevalent and pernicious influence, and the establishment of obesity as a true medical condition defends against this in the form of legitimacy. The codification of obesity as a disease implies that, as with other diseases, it is (at least relatively) inappropriate to "blame the victim."

Of perhaps more direct practical importance is that the identification of obesity as a disease facilitates its inclusion among conditions with medical insurance coverage. The *International Classification of Diseases* (ICD) coding system used for billing third-party payers assigns a "diagnostic code" to any given condition. Obesity must be recognized among candidate conditions for such coverage to be processed. The U.S. Department of Health and Human Services initially designated obesity as a disease with this in mind, and relevant progress has followed. In 2011 the Centers for Medicare and Medicaid Services (CMS) authorized reimbursement for

obesity counseling to physicians treating patients with a body mass index (BMI) of 30 or greater[25] (Table 19-1).

There is a potential liability, however, in cataloging obesity as a disease. Diseases are states of aberrant body function generally amenable to medical treatments (e.g., pharmacotherapy, surgery). If obesity constitutes such an aberrant state, it invites a focus on such treatments as bariatric surgery and antiobesity drugs. The effectiveness of bariatric surgery is well established and the pursuit of effective drugs for weight management well justified, but a dedicated focus on these approaches can and likely does distract attention and divert resources from policies and programs that facilitate better use of feet and forks. In other words, by *blaming* obesity on a diseased state of the body, the potential to address the *diseased* state of the **obesigenic** (obesity-causing) environment may be diminished.

An analogy well suited to clarify this perspective is drowning. Drowning is a legitimate medical condition for which medical care is warranted and for which both diagnostic codes and reimbursement are available. However, no one mistakes the propensity to drown as an "aberrant state of the body." Rather, a perfectly normal and healthy body is simply not suited to breathing under the water. Drowning (or near-drowning) is recognized universally as the inevitable outcome when a normal body spends too much time in an environment (underwater) to which it is poorly suited. The importance of this perspective is in how it relates to prevailing societal responses. The treatment of drowning after it occurs is relatively rare and far from optimal. Many routine steps are taken—from posting lifeguards at beaches, to teaching children how to swim, to putting fences around pools—to prevent drowning from occurring. Only when the clear emphasis on environmental approaches to prevention fails does the treatment of drowning become germane, as a last resort.

Throughout most of human history, calories have been relatively scarce and often difficult to obtain, and physical activity has been an unavoidable requirement for survival. Modern society has devised an environment in which physical activity is scarce and often difficult to maintain, and calories are unavoidable. Homo sapiens are endowed with no native defenses against caloric excess and the tendency toward "sedentariness." The result is the modern obesity trends. In essence, the population is confronting an environment for which it is poorly suited and is succumbing to its toxic effects. We are *drowning* in calories. This perspective might promote an emphasis on environmentally based approaches (policies and programs that facilitate healthful eating and routine physical activity) to obesity prevention and control, even while establishing the medical legitimacy of obesity as a condition deserving treatment (Box 19-3).

Nonmodifiable risk factors for obesity include low resting energy expenditure, genetic polymorphisms that predispose to weight gain and impede weight loss, and an ethnic heritage that increases the propensity for obesity. *Modifiable* risk factors relate principally to the quality and quantity of dietary intake and energy expenditure through exercise. Lean body mass can be increased through exercise and thus also constitutes a modifiable risk factor. Insomnia increases obesity risk by several mechanisms, and thus impaired sleep is a potentially modifiable risk factor as well.

The primary and secondary prevention of obesity principally involve improvements in diet and physical activity patterns. Secondary prevention includes screening, which means clinical assessment of weight and height (BMI) as well as waist circumference, and for children the plotting of BMI on appropriate growth charts.[26]

Table 19-1 Classification of Weight Status Based on Body Mass Index (BMI)

BMI*	Classification
<18	Underweight
18-25	Normal weight
25-29.9	Overweight
30-34.9	Stage I obesity
35-39.9	Stage II obesity
>40	Stage III (severe) obesity

*Expressed as weight in kilograms divided by the square of the height in meters (weight [kg]/height^2 [m]).

Box 19-3 Summary of Obesity Risk Factors and Prevention*

Risk Factors

Nonmodifiable
Resting energy expenditure/basal metabolic rate
Genetics
Ethnicity

Modifiable
Energy consumption
Energy expenditure
Lean body mass
Sleep quality and quantity

Primary Prevention

Dietary management: improved quality, control of quantity
Physical activity

Secondary Prevention

Screening: Assessing body mass index (BMI) and waist circumference in clinical practice; plotting pediatric BMI on growth charts
Dietary management
Physical activity promotion
Possible use of pharmacotherapy

Tertiary Prevention

Bariatric surgery
Pharmacotherapy
Dietary management and physical activity promotion as important adjuncts

*Primary prevention is for nonobese individuals to prevent them from becoming obese. Secondary prevention is for asymptomatically obese individuals. Tertiary prevention is for symptomatic obesity.

Tertiary prevention, to prevent complications of established obesity, often involves pharmacotherapy for metabolic complications and bariatric surgery. The utility of bariatric surgery is well established. Pharmacotherapy for obesity is, to date, of limited utility and prone to unintended consequences. The use of medications for the metabolic complications of obesity, such as prediabetes, is more clearly supported by high-quality evidence.[27]

Figure 19-2 shows the prevalence of obesity in low-income U.S. children age 2 to 4 years.

See Figure 19-3 on studentconsult.com for obesity trends in U.S. adults. (For USPSTF recommendations on obesity, see the Websites list at end of chapter.)

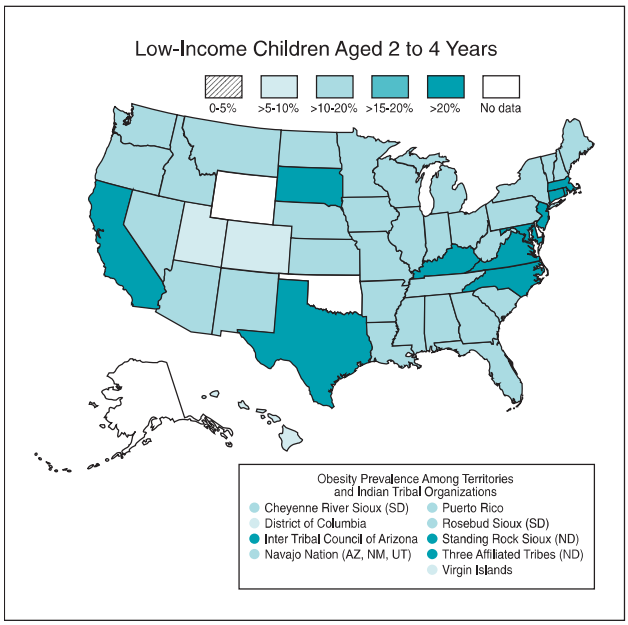

Figure 19-2 Obesity prevalence in early childhood, United States, 2009. Among low-income children age 2 to 4 years by state. *Insert,* In territories and Indian tribe organizations. (From Division of Nutrition, Physical Activity and Obesity, National Center for Chronic Disease Prevention and Health Promotion, Atlanta, 2009, US Centers for Disease Control and Prevention.)

B. Type 2 Diabetes Mellitus

In developed countries, about 95% of patients with diabetes mellitus have type 2. Whereas **type 1 diabetes** is an autoimmune disease resulting in destruction of the insulin-producing beta cells of the islets of Langerhans, type 2 diabetes is overwhelmingly a lifestyle-related disease of progressive insulin resistance mediated largely by excess body fat. Type 2 diabetes mellitus, formerly called "adult-onset diabetes," is usually preventable, both by treating the insulin resistance that often precedes it and, more fundamentally, by preventing the accumulation of excess visceral fat that is an important root cause, if not the cause, in most patients.[27]

The importance of preventing type 2 diabetes is reflected in its large contribution to current health care costs and the projections of its future prevalence. The CDC projects that as many as one in three Americans will have diabetes by the mid–21st century if current trends persist,[28] putting the fate of the U.S. health care system in doubt. Fortunately, type 2 diabetes is overwhelmingly preventable by available interventions. A fasting glucose between 100 and 125 mg/dL is indicative of **prediabetes,** whereas a level of 126 mg/dL or greater indicates diabetes.[29] The U.S. Preventive Services Task Force (USPSTF) specifically recommends diabetes screening in patients with borderline or overt hypertension.[30]

Risk factors for type 2 diabetes overlap substantially with risk factors for obesity. Rates of diabetes are considerably higher in some ethnic groups than others, and there is a known genetic predisposition. The principal driver of the epidemiology of type 2 diabetes, however, and its progression from a disease of adults into a disease of children and adults alike, is **epidemic** (or hyperendemic) **obesity.** The epidemiology of obesity has changed drastically over recent decades; genes have not. In particular, central adiposity and the accumulation of excess visceral fat in the liver are causally implicated. Diabetes can be prevented with lifestyle interventions that foster moderate weight loss; with pharmacotherapy; and with bariatric surgery. Medical management of diabetes to prevent progression and complications constitutes tertiary prevention. Box 19-4 summarizes these issues.

Box 19-4 Summary of Type 2 Diabetes Risk Factors and Prevention

Risk Factors

Nonmodifiable
Genetics
Ethnicity

Modifiable
Obesity, in particular abdominal (visceral) adiposity

Primary Prevention

Weight loss/management
Dietary management
Physical activity
Pharmacotherapy
Bariatric surgery

Secondary Prevention

Screening: Fasting glucose; glucose tolerance testing
Dietary management
Physical activity
Pharmacotherapy
Bariatric surgery

Tertiary Prevention

Pharmacotherapy
Medical assessment for potential complications (e.g., eye and foot examinations)
Bariatric surgery
Weight loss/management
Dietary management
Physical activity

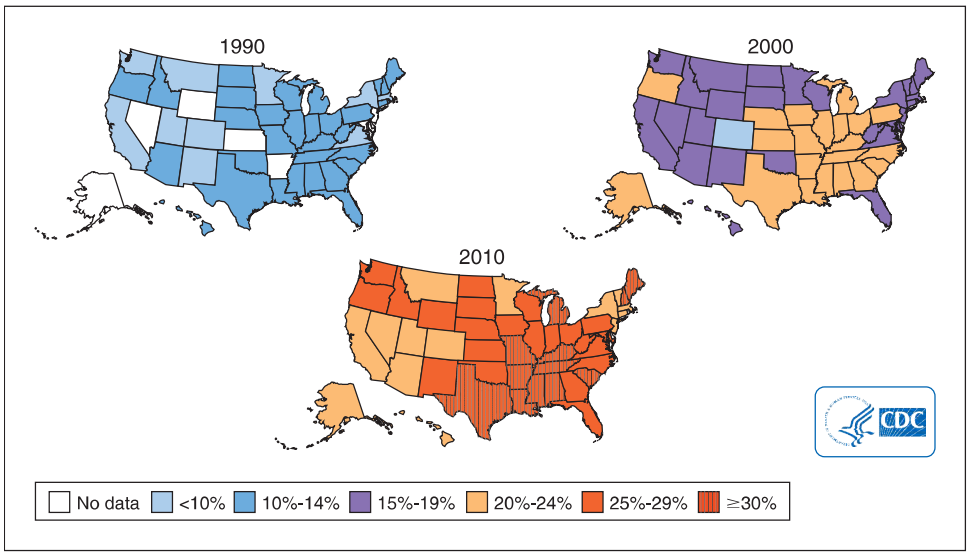

Figure 19-3 Obesity trends* among U.S. adults: 1990, 2000, 2010. (From Behavioral Risk Factor Surveillance System [BRFSS], Atlanta, 2010, Centers for Disease Control and Prevention [CDC].) *BMI≥30, or about 30 pounds overweight for a 5′4″ person.

C. Stroke (Cerebrovascular Accident)

Stroke, or cerebrovascular accident (CVA), is the fourth leading cause of death in the United States after heart disease, cancer, and lung disease[31] and a major cause of long-term morbidity. The incidence rate of stroke in those age 50 and older had declined in the United States, principally because of better detection and treatment of hypertension, the major risk factor.[32] The morbidity of stroke has been somewhat attenuated through the use of thrombolytic therapy that can restore blood flow and salvage brain tissue imperiled by ischemia. **Hemorrhagic stroke** is a potential side effect of such therapies and can occur independently of them. Hemorrhagic stroke is much less common than ischemic stroke, less predictable, and in general less preventable.

A marked rise in the rate of stroke in children age 5 to 14 years has been observed recently in the United States.[32] The explanation is uncertain, but childhood obesity is cited as a likely candidate.

Risk factors for stroke overlap substantially with risk factors for cardiovascular disease (see next). Medical conditions (e.g., diabetes) that increase the risk of heart disease similarly increase the risk of stroke. Atrial fibrillation is a risk factor for stroke, generally managed with anticoagulation. The main modifiable risk factor for stroke is **hypertension.** Patient adherence to management guidelines for blood pressure reliably translates into reduced stroke risk and, at the population level, reduced stroke incidence.

Revascularization, such as carotid endarterectomy after a transient ischemic attack, constitutes secondary stroke prevention. Thrombolytic and anticoagulant therapies to limit stroke-related injury to the brain and rehabilitation programs to preserve and restore function constitute the mainstays of tertiary prevention. Updated information about stroke management and prevention is available from the CDC[33] and the American Stroke Foundation.[34] As of January 2012, the USPSTF recommends against screening for carotid stenosis in asymptomatic individuals.[35]

D. Cardiovascular Disease

Cardiovascular disease has long been the leading cause of death in both men and women in the United States and remains so at this time.[36] It exerts a comparable toll in developed countries worldwide and causes a high and rising number of deaths globally.[37]

Risk factors for heart disease vary by culture and circumstance. In some parts of the world, infectious disease, such as streptococcal pharyngitis leading to rheumatic fever, or Chagas' disease resulting from infection by *Trypanosoma cruzi* in South America,[38] remains an important cause of heart disease. The focus here is preferentially on the epidemiology of heart disease, specifically **coronary artery disease** (CAD), or coronary heart disease, in the United States and comparably developed nations, in which the role of infection is minor (although not inconsequential). Chronic inflammation is now known to propagate the progression of atherosclerotic plaque, implicating such conditions as periodontal disease (see later).

The principal determinants of cardiovascular risk tend to be lifestyle behaviors. In particular, tobacco use, dietary pattern, and physical activity level are of considerable importance and greatly influence the probability of future cardiac events (e.g., unstable angina, heart attacks, sudden cardiac death). To some extent, however, such effects are indirect. Poor diet and lack of physical activity tend to contribute to dyslipidemia and hypertension, which in turn raise cardiovascular risk. It is these "downstream effects" of diet and physical activity patterns that are incorporated into quantified estimates of future risk, such as the Framingham cardiac risk score.[39]

Box 19-5 summarizes cardiovascular risk factors and prevention strategies. Many risk factors contribute to cardiovascular disease, including age, gender, hypertension, smoking, and dyslipidemia.[40] Of the modifiable risk factors, a serum cholesterol level greater than 181 mg/dL, systolic blood pressure greater than 120 mm Hg, smoking, and history of

Box 19-5 Summary of Cardiovascular Disease Risk Factors and Prevention

Risk Factors

Nonmodifiable
Age
Gender
Family history/genetics

Modifiable
Dyslipidemia
Hypertension
Diabetes/prediabetes (including insulin resistance)
Obesity, in particular abdominal (visceral) adiposity
Poor diet
Lack of physical activity
Smoking
Stress

Primary Prevention

Tobacco avoidance
Healthful eating
Physical activity
Stress management
Weight control
Pharmacotherapy for risk factor modification (e.g., hypertension, diabetes, dyslipidemia)
Risk factor screening (e.g., cholesterol, blood pressure)

Secondary Prevention

Risk factor management, as for primary prevention
Revascularization (angioplasty; coronary artery bypass surgery)

Tertiary Prevention

Risk factor management as for primary prevention to prevent recurrence/progression
Revascularization to preserve/restore function
Cardiac rehabilitation

diabetes together explain about 87% of coronary heart disease (CHD) risk.[41] However, the impact of changing these risk factors has variable impact on total risk. For example, for CAD, cigarette smoking increases the risk for smokers by 70% versus nonsmokers. In contrast, a long-term change of 23 mg/dL of serum cholesterol in men age 55 to 64 reduced congestive heart failure (CHF) risk by 25%. A 5–mm Hg change in diastolic blood pressure decreases CHD risk by 21%.[41] Also, risk factors have different weight on different manifestations; dyslipidemia is a stronger risk factor for CAD and peripheral artery disease (PAD) than for stroke and CHF, hypertension is more important for stroke and CHF, and smoking has the strongest impact on PAD risk.[40]

These risk factors do not act independently, and other factors, such as stress, socioeconomic status, and family history are often not captured in these studies. Also, concentrating on one risk factor at a time carries the risk of underestimating cardiovascular disease (CVD) risk in patients with multiple marginal risk factors. The best way to estimate risk is to use validated total risk score such as the Framingham risk calculator, which allows one to estimate the 10-year risk for CVD based on a combination of age, gender, and risk factors levels. In the past, there was a different risk calculator for CAD, stroke, and CHF. In 2008 a risk score for general CVD risk was published, the Framingham Heart Study general cardiovascular disease: 10-year risk,[42] which performs as well as the individual disease calculators. This score also provides a *risk age,* the biologic age that corresponds to the risk level of a patient, which is useful in communicating risk to patients. For example, if a patient is 40 years old but his risk age is 80, his cardiovascular risk is as high as if he were 80 years old. (A discussion of comprehensive cardiac risk modification is beyond the scope of this chapter.)

Epidemiologic research reports that at least 80% of all CAD is preventable by addressing a short list of lifestyle-related risk factors, notably dietary pattern, physical activity pattern, and tobacco use. Similar risk reductions are likely possible at later stages with pharmacologic management of risk factors, such as antihypertensive medications, statins (cholesterol-lowering drugs) and other drugs for dyslipidemia, and platelet inhibition with aspirin.[43] The emphasis for prevention is on lifestyle behaviors before the development and progression of risk factors, shifting toward pharmacotherapy as risk factors progress.

See Table 19-3 on studentconsult.com for a summary of lipid management recommendations of the National Heart, Lung, and Blood Institute of the NIH.

The field of cardiovascular medicine evolves rapidly, and thus readers are referred to the peer-reviewed literature and authoritative websites for up-to-date information regarding epidemiology, prevention, and treatment. Key areas at present include the detection and management of cardiac risk factors in adolescents and children; the optimal use of statins in men and women for primary prevention; the utility of diverse biomarkers of cardiac risk; and the incremental utility of various risk assessment modalities, such as coronary computed tomography (CT) imaging.

E. Chronic Lung Disease

Chronic lower respiratory tract disease, including chronic obstructive pulmonary disease (COPD), emphysema, bronchitis, and pneumoconiosis constitutes the third leading cause of death in the United States after heart disease and cancer.[44] An enormous portion of this toll is directly related to tobacco and is thus preventable with tobacco avoidance. Pneumoconioses are generally work-related diseases, and prevention is thus an occupational health issue (see Chapter 22). Asthma, an important chronic condition of the upper airway, is a relatively uncommon cause of mortality but an important cause of morbidity.

Nonmodifiable risk factors for chronic pulmonary disease include age and certain genetic disorders, such as α_1-antitrypsin deficiency[45] and cystic fibrosis.[46] Modifiable risk factors include exposure to airborne toxins caused by pollution, occupation, or tobacco smoke.

Tobacco avoidance and smoking cessation are top priorities in the prevention and treatment of chronic pulmonary diseases. There is no standard screening for pulmonary disease. The USPSTF recommends against screening for COPD[47] and currently is noncommittal about lung cancer screening,[48] a subject of ongoing study prone to change. Secondary prevention thus relates to management of early-stage disease to prevent progression. Pharmacotherapy is prominent in such efforts, notably antiinflammatory drugs (e.g., steroids) for asthma, COPD, and chronic bronchitis. Tertiary prevention may include home oxygen for patients functionally limited by hypoxemia, along with medications to manage symptoms and prevent progression, and pulmonary rehabilitation after decompensation. Both the CDC[49] and the American Lung Association[50] provide patient-friendly guidance online. The National Heart, Lung, and Blood Institute (NHLBI) provides a useful source of regularly updated information for health professionals.[51]

F. Cancer

Unlike most chronic diseases, which pertain to a particular organ system (e.g., heart disease, stroke, pulmonary disease, arthritis, diabetes), cancer—the second leading cause of death in the United States[52]—can affect any organ or tissue in the body and is relatively common and potentially lethal. Thus the topic is vast; comprehensive detail is available elsewhere, notably oncology textbooks and journals. The most important facts about cancer include the following:

- Cancer is acknowledged to be substantially (up to 60%) preventable by addressing lifestyle behaviors.
- Cancer is not the unpredictable threat that the public tends to believe it is.

Cancer development is a predictable process, analogous to the progression of atherosclerotic plaque leading to clinically significant coronary disease. The steps of that process span years to decades, with opportunity for effective prevention (Table 19-2). *Initiation* refers to the development of a potentially carcinogenic (cancer-causing) mutation. *Promotion* refers to the growth of cancer cells, before any clinical symptoms or signs develop. *Expression* refers to the first clinical evidence of the presence of cancer.

Nonmodifiable risk factors for cancer include age and predisposing genetic mutations, some of which are prevalent, important, and well known (e.g., *BRCA*).[53] Modifiable risk factors include diet, physical activity, body weight, tobacco use, exposure to infectious agents, and toxins.

ATP III Guidelines At-A-Glance Quick Desk Reference

Step 1

Determine lipoprotein levels–obtain complete lipoprotein profile after 9- to 12-hour fast.

ATP III Classification of LDL, Total, and HDL Cholesterol (mg/dL)

LDL Cholesterol – Primary Target of Therapy	
<100	Optimal
100-129	Near optimal/above optimal
130-159	Borderline high
160-189	High
≥190	Very high
Total Cholesterol	
<200	Desirable
200-239	Borderline high
≥240	High
HDL Cholesterol	
<40	Low
≥60	High

Step 2

Identify presence of clinical atherosclerotic disease that confers high risk for coronary heart disease (CHD) events (CHD risk equivalent):

- Clinical CHD
- Symptomatic carotid artery disease
- Peripheral arterial disease
- Abdominal aortic aneurysm.

Step 3

Determine presence of major risk factors (other than LDL):

Major Risk Factors (Exclusive of LDL Cholesterol) That Modify LDL Goals

Cigarette smoking
Hypertension (BP ≥140/90 mmHg or on antihypertensive medication)
Low HDL cholesterol (<40 mg/dL)*
Family history of premature CHD (CHD in male first degree relative <55 years; CHD in female first degree relative <65 years)
Age (men ≥45 years; women ≥55 years)

** HDL cholesterol ≥60 mg/dL counts as a "negative" risk factor; its presence removes one risk factor from the total count.*

- Note: in ATP III, diabetes is regarded as a CHD risk equivalent.

4

Step 4

If 2+ risk factors (other than LDL) are present without CHD or CHD risk equivalent, assess 10-year (short-term) CHD risk (see Framingham tables).
Three levels of 10-year risk:

- >20% — CHD risk equivalent
- 10-20%
- <10%

5

Step 5

Determine risk category:

- Establish LDL goal of therapy
- Determine need for therapeutic lifestyle changes (TLC)
- Determine level for drug consideration

LDL Cholesterol Goals and Cutpoints for Therapeutic Lifestyle Changes (TLC) and Drug Therapy in Different Risk Categories.

Risk Category	LDL Goal	LDL Level at Which to Initiate Therapeutic Lifestyle Changes (TLC)	LDL Level at Which to Consider Drug Therapy
CHD or CHD Risk Equivalents (10-year risk >20%)	<100 mg/dL	≥100 mg/dL	≥130 mg/dL (100-129 mg/dL: drug optional)*
2+ Risk Factors (10-year risk ≤20%)	<130 mg/dL	≥130 mg/dL	10-year risk 10-20%: ≥130 mg/dL 10-year risk <10%: ≥160 mg/dL
0-1 Risk Factor†	<160 mg/dL	≥160 mg/dL	≥190 mg/dL (160-189 mg/dL: LDL-lowering drug optional)

* *Some authorities recommend use of LDL-lowering drugs in this category if an LDL cholesterol <100 mg/dL cannot be achieved by therapeutic lifestyle changes. Others prefer use of drugs that primarily modify triglycerides and HDL, e.g., nicotinic acid or fibrate. Clinical judgment also may call for deferring drug therapy in this subcategory.*

† *Almost all people with 0-1 risk factor have a 10-year risk <10%, thus 10-year risk assessment in people with 0-1 risk factor is not necessary.*

6

Step 6

Initiate therapeutic lifestyle changes (TLC) if LDL is above goal.

TLC Features

- TLC Diet:
  - Saturated fat <7% of calories, cholesterol <200 mg/day
  - Consider increased viscous (soluble) fiber (10-25 g/day) and plant stanols/sterols (2g/day) as therapeutic options to enhance LDL lowering
- Weight management
- Increased physical activity.

7

Step 7

Consider adding drug therapy if LDL exceeds levels shown in Step 5 table:

- Consider drug simultaneously with TLC for CHD and CHD equivalents
- Consider adding drug to TLC after 3 months for other risk categories.

Drugs Affecting Lipoprotein Metabolism

Drug Class	Agents and Daily Doses	Lipid/Lipoprotein Effects		Side Effects	Contraindications
HMG CoA reductase inhibitors (statins)	Lovastatin (20-80 mg) Pravastatin (20-40 mg) Simvastatin (20-80 mg) Fluvastatin (20-80 mg) Atorvastatin (10-80 mg) Cerivastatin (0.4-0.8 mg)	LDL HDL TG	↓18-55% ↑5-15% ↓7-30%	Myopathy Increased liver enzymes	Absolute: • Active or chronic liver disease Relative: • Concomitant use of certain drugs*
Bile acid sequestrants	Cholestyramine (4-16 g) Colestipol (5-20 g) Colesevelam (2.6-3.8 g)	LDL HDL TG	↓15-30% ↑3-5% No change or increase	Gastrointestinal distress Constipation Decreased absorption of other drugs	Absolute: • dysbeta-lipoproteinemia • TG >400 mg/dL Relative: • TG >200 mg/dL
Nicotinic acid	Immediate release (crystalline) nicotinic acid (1.5-3 gm), extended release nicotinic acid (Niaspan®) (1-2 g), sustained release nicotinic acid (1-2 g)	LDL HDL TG	↓5-25% ↑15-35% ↓20-50%	Flushing Hyperglycemia Hyperuricemia (or gout) Upper GI distress Hepatotoxicity	Absolute: • Chronic liver disease • Severe gout Relative: • Diabetes • Hyperuricemia • Peptic ulcer disease
Fibric acids	Gemfibrozil (600 mg BID) Fenofibrate (200 mg) Clofibrate (1000 mg BID)	LDL *(may be increased in patients with high TG)* HDL TG	↓5-20% ↑10-20% ↓20-50%	Dyspepsia Gallstones Myopathy	Absolute: • Severe renal disease • Severe hepatic disease

* *Cyclosporine, macrolide antibiotics, various anti-fungal agents, and cytochrome P-450 inhibitors (fibrates and niacin should be used with appropriate caution).*

8

Step 8

Identify metabolic syndrome and treat, if present, after 3 months of TLC.

Clinical Identification of the Metabolic Syndrome – Any 3 of the Following:

Risk Factor	Defining Level
Abdominal obesity*	Waist circumference†
Men	>102 cm (>40 in)
Women	>88 cm (>35 in)
Triglycerides	≥150 mg/dL
HDL cholesterol	
Men	<40 mg/dL
Women	<50 mg/dL
Blood pressure	≥130/≥85 mmHg
Fasting glucose	≥110 mg/dL

* *Overweight and obesity are associated with insulin resistance and the metabolic syndrome. However, the presence of abdominal obesity is more highly correlated with the metabolic risk factors than is an elevated body mass index (BMI). Therefore, the simple measure of waist circumference is recommended to identify the body weight component of the metabolic syndrome.*

† *Some male patients can develop multiple metabolic risk factors when the waist circumference is only marginally increased, e.g., 94-102 cm (37-39 in). Such patients may have a strong genetic contribution to insulin resistance. They should benefit from changes in life habits, similarly to men with categorical increases in waist circumference.*

Treatment of the metabolic syndrome

- Treat underlying causes (overweight/obesity and physical inactivity):
  - Intensify weight management
  - Increase physical activity.

- Treat lipid and non-lipid risk factors if they persist despite these lifestyle therapies:
  - Treat hypertension
  - Use aspirin for CHD patients to reduce prothrombotic state
  - Treat elevated triglycerides and/or low HDL (as shown in Step 9).

9

Step 9

Treat elevated triglycerides.

ATP III Classification of Serum Triglycerides (mg/dL)

<150	Normal
150-199	Borderline high
200-499	High
≥500	Very high

Treatment of elevated triglycerides (≥150 mg/dL)

- Primary aim of therapy is to reach LDL goal
- Intensify weight management
- Increase physical activity
- If triglycerides are ≥200 mg/dL after LDL goal is reached, set secondary goal for non-HDL cholesterol (total – HDL) 30 mg/dL higher than LDL goal.

Comparison of LDL Cholesterol and Non-HDL Cholesterol Goals for Three Risk Categories

Risk Category	LDL Goal (mg/dL)	Non-HDL Goal (mg/dL)
CHD and CHD Risk Equivalent (10-year risk for CHD >20%)	<100	<130
Multiple (2+) Risk Factors and 10-year risk ≤20%	<130	<160
0-1 Risk Factor	<160	<190

If triglycerides 200-499 mg/dL after LDL goal is reached, consider adding drug if needed to reach non-HDL goal:

- intensify therapy with LDL-lowering drug, or
- add nicotinic acid or fibrate to further lower VLDL.

If triglycerides ≥500 mg/dL, first lower triglycerides to prevent pancreatitis:

- very low-fat diet (≤15% of calories from fat)
- weight management and physical activity
- fibrate or nicotinic acid
- when triglycerides <500 mg/dL, turn to LDL-lowering therapy.

Treatment of low HDL cholesterol (<40 mg/dL)

- First reach LDL goal, then:
- Intensify weight management and increase physical activity
- If triglycerides 200-499 mg/dL, achieve non-HDL goal
- If triglycerides <200 mg/dL (isolated low HDL) in CHD or CHD equivalent consider nicotinic acid or fibrate.

Men

Estimate of 10-Year Risk for Men

(Framingham Point Scores)

Age	Points
20-34	-9
35-39	-4
40-44	0
45-49	3
50-54	6
55-59	8
60-64	10
65-69	11
70-74	12
75-79	13

Total Cholesterol	Points				
	Age 20-39	Age 40-49	Age 50-59	Age 60-69	Age 70-79
<160	0	0	0	0	0
160-199	4	3	2	1	0
200-239	7	5	3	1	0
240-279	9	6	4	2	1
≥280	11	8	5	3	1

	Points				
	Age 20-39	Age 40-49	Age 50-59	Age 60-69	Age 70-79
Nonsmoker	0	0	0	0	0
Smoker	8	5	3	1	1

HDL (mg/dL)	Points
≥60	-1
50-59	0
40-49	1
<40	2

Systolic BP (mmHg)	If Untreated	If Treated
<120	0	0
120-129	0	1
130-139	1	2
140-159	1	2
≥160	2	3

Point Total	10-Year Risk %
<0	< 1
0	1
1	1
2	1
3	1
4	1
5	2
6	2
7	3
8	4
9	5
10	6
11	8
12	10
13	12
14	16
15	20
16	25
≥17	≥ 30

10-Year risk _____%

Women

Estimate of 10-Year Risk for Women

(Framingham Point Scores)

Age	Points
20-34	-7
35-39	-3
40-44	0
45-49	3
50-54	6
55-59	8
60-64	10
65-69	12
70-74	14
75-79	16

Total Cholesterol	Points				
	Age 20-39	Age 40-49	Age 50-59	Age 60-69	Age 70-79
<160	0	0	0	0	0
160-199	4	3	2	1	1
200-239	8	6	4	2	1
240-279	11	8	5	3	2
≥280	13	10	7	4	2

	Points				
	Age 20-39	Age 40-49	Age 50-59	Age 60-69	Age 70-79
Nonsmoker	0	0	0	0	0
Smoker	9	7	4	2	1

HDL (mg/dL)	Points
≥60	-1
50-59	0
40-49	1
<40	2

Systolic BP (mmHg)	If Untreated	If Treated
<120	0	0
120-129	1	3
130-139	2	4
140-159	3	5
≥160	4	6

Point Total	10-Year Risk %
< 9	< 1
9	1
10	1
11	1
12	1
13	2
14	2
15	3
16	4
17	5
18	6
19	8
20	11
21	14
22	17
23	22
24	27
≥25	≥ 30

10-Year risk _____%

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
National Institutes of Health
National Heart, Lung, and Blood Institute

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Table 19-2 Steps in Development and Progression of Cancer and Opportunities for Prevention

Stage	Relevant Prevention Methods
Initiation	Toxin avoidance, particularly tobacco smoke and excess alcohol Healthful diet Weight control Physical activity Immunization, in some cases
Promotion	Early detection and treatment through screening Other methods as for initiation
Expression	Diagnosis and treatment Other methods as for initiation

The primary prevention of cancer mostly involves the avoidance of relevant pathogens, including the following:

- Human papillomavirus (HPV), implicated in cervical cancer, anal and penile cancers, and head and neck cancers
- Hepatitis B virus (HBV), implicated in hepatocellular carcinoma
- Toxins, such as tobacco and excess alcohol
- Industrial chemicals at the worksite and potentially contaminating the environment and food supply

In theory, organically grown food offers benefits in this regard, but establishing such evidence is difficult and largely nascent to date. Healthful eating, moderate physical activity, and weight control offer important defenses at all stages of cancer. As noted in the previous discussion of obesity, the link between excess body fat and cancer risk is well established and of general importance.[54] In select patients, immunization may serve as primary cancer prevention by preventing an initiating infection (e.g., against HPV and HBV).

The secondary prevention of cancer principally involves making use of effective screening protocols. The USPSTF recommends screening specific populations for cervical, breast, and colon cancers; recommends against screening for some others; and is noncommittal in certain cases, such as lung cancer, where evidence is equivocal and evolving.[55] Readers are encouraged to keep current with these often-changing topics by visiting the USPSTF website (see Chapter 18).

Tertiary cancer prevention involves effective treatment and a range of strategies aimed at preventing recurrence and progression, as well as strategies to restore function or appearance, such as rehabilitation and reconstructive cosmetic surgery. This topic potentially encompasses all aspects of cancer treatment. One example of tertiary prevention incorporated into treatment is hormonal therapy to prevent recurrence, applied notably to prostate and breast cancer. The selective estrogen receptor modulators, such as tamoxifen and raloxifene, substantially reduce breast cancer incidence. Raloxifene, approved for treating and preventing osteoporosis, may also be used for primary breast cancer prevention in high-risk women.[56]

G. Oral Health

Dental caries is one of the few conditions so common without routine care that screening is inappropriate. Instead, prophylaxis in the form of routine dental visits and cleanings, with fluoride application, is the standard of care.

In addition to caries, periodontal disease is an important form of pathology in the oral cavity. Research over recent decades has highlighted the importance of oral health to general health and the link between gingivitis and periodontitis to a variety of systemic diseases.[57] The following primary strategies help prevent chronic disease of the oral cavity:

- Good oral hygiene (routine brushing and flossing)
- Adequate intake of fluoride from water or dental treatment
- Routine dental visits
- Avoidance of excess alcohol
- Avoidance of toxins, such as tobacco

H. Dementia, Chronic Pain, and Arthritis

Other chronic conditions include dementias, back pain, recurrent headaches, neuropathies, rheumatologic disease, and atopic conditions.

Dementia is a diverse category of conditions; some are preventable by means as simple as nutrient supplementation, and others are not known to be preventable at all. Alzheimer's disease is of particular interest in this regard. Because of its rising prevalence, related in part to an aging population, and its enormous human and economic costs, Alzheimer's disease is receiving increasing attention, and resources related to prevention, early diagnosis, treatment, and cure. To the extent currently thought possible, Alzheimer's disease is preventable generally through the prevention of cardiovascular disease.[58]

Conditions of **chronic pain,** especially arthritis, are prevalent and important contributors to morbidity, [59-61] as well as indirectly to mortality. For example, the physical inactivity leading to progression of obesity and development of diabetes may be a major determinant of a fatal myocardial infarction. With the potential interplay of chronic conditions, each compounding the other, chronic pain may foster physical inactivity, which may lead to weight gain, which may exacerbate the pain. Such complexity occurs in many older patients with chronic disease, warranting meaningful applications of *holistic care.*[62]

Osteoarthritis (OA) may be the quintessential example of a degenerative disease attributable to "wear and tear." Symptoms develop and progress as friction erodes articular cartilage in the knee, hip, hand, and other joints. Some degree of secondary inflammation may occur, but inflammation is relatively unimportant in OA, in contrast to rheumatologic diseases such as rheumatoid arthritis. Strategies for the primary prevention of OA include avoiding excessive stress to joints and exercising to keep muscles well conditioned. Secondary prevention directed at symptom control and preservation of function involves analgesics, supplements, and modalities such as massage, as well as regular physical activity. Tertiary prevention—restoration of function impaired by disease progression and prevention of complications—includes physical therapy and rehabilitation, strategies to reconstitute eroded cartilage, and surgery, especially joint replacement. Relevant reviews are available for clinicians,[63] as are online sources for patients.[64]

IV. BARRIERS AND OPPORTUNITIES

A. Impediments to Chronic Disease Prevention

The toll of chronic disease and its well-established preventability by available means make a compelling case for action, especially considering the personal nature of public health statistics. Almost every family in modern society has faced some prevalent chronic disease and knows someone with heart disease, cancer, lung disease, stroke, or diabetes. If we were to find the means to turn what we know about prevention into what we practice routinely, up to 8 in 10 persons directly affected by chronic disease would not have been.[65] We as a society have the opportunity to bequeath the avoidance of that suffering and loss to our children. One barrier that might be readily overcome is the failure to part the veil of statistical anonymity and recognize the familiar faces on the other side.

1. Personal Barriers

Other barriers to fulfilling the promise of chronic disease prevention relate to lifestyle behaviors. The three leading root causes of chronic disease are tobacco use, poor diet, and lack of physical activity. Medical intervention is at best only a partial response to any of these. Patients can be supported in a smoking cessation effort, but they still must be willing to undergo the effort. Healthful diet and routine exercise may be recommended, but patients must make a longitudinal commitment to both. As the focus of prevention moves outside the clinical domain, health professionals have less direct control. Therefore an important barrier is that chronic disease prevention increasingly must be a personal endeavor, and many people lack the required skill or the will, or both.

2. Public Barriers

Many aspects of modern living conspire directly against chronic disease prevention efforts. Overconsumption of calories is routine for many reasons, including federal subsidies that foster the propagation of processed foods, the willful hyperpalatability of these foods, assertive and creative food-marketing efforts, and the ubiquity of food (especially fast food). Lack of physical activity is explained in part by an ever-expanding array of devices that perform tasks once done by muscles, at work and at play, with schedules that make the allocation of time for exercise difficult and excuses easy. In essence, almost everything about modern living that makes it modern is obesigenic, and much is **morbidigenic** (disease-causing).[66]

B. Opportunities for Chronic Disease Prevention

Opportunities, however, are as great and numerous as barriers and challenges. There is increasing attention to the importance of prevention for both the public health and the health of national economies. Federal regulations, such as reimbursement for lifestyle counseling by physicians, are evolving.[25] A medical specialty devoted to lifestyle approaches has emerged,[67] and "new age" tools provide novel means to engage health care professionals in effective behavior modification efforts.[68]

Given the traditional focus of formalized medicine on *disease care*, it is not surprising that much of the emphasis on prevention in the health care context relates to better screening, early treatment, and better management of established chronic disease. Two examples are the patient-centered medical home[11] and the chronic care model.[12] Both are designed to improve the flow of information, with the patient at the center and the goal to improve delivery of care so that outcomes are enhanced and costs reduced. Another important concept is that delivery and receipt of clinical preventive services can be enhanced by engaging nonclinical, community-based entities as partners.[69]

Although laudable and important, these models emphasize the delivery of clinical services and define the recipient as a patient. The greatest opportunities for chronic disease prevention (1) involve changing lifestyle behaviors in ways that are acceptable to most people, (2) reside largely outside the clinical setting, and (3) relate to the preservation of health in people who have no cause to be "patients."

Clinicians can learn to be more effective agents of change, but only to a certain degree. Various health-related policies could be adopted to facilitate favorable "defaults."[70] Expert guidance may be provided at decision points, such as the purchase of food.[71] Financial incentives may be used to motivate achievement of health goals[72] or to reward healthful choices.[73] The financial interest of businesses in workforce health promotion may be better leveraged to advance health promotion in other settings as well.[74]

The promise of drastic reductions in the human and financial costs of chronic disease beckons and is achievable by means already in hand. The challenge our society now confronts is to muster the resolve to traverse the miles that separate what we know about chronic disease prevention from what we do.

V. SUMMARY

The human and financial toll of chronic disease in modern society presents many opportunities for prevention, particularly in regard to the short list of factors responsible for most chronic diseases, directly or indirectly. This same list indicates the degree to which all or most chronic diseases could be prevented through one common, health-promoting approach, a promise borne out by population studies. As much as an 80% reduction in the mortality and morbidity of heart disease, cancer, pulmonary disease, stroke, and diabetes could be achieved with improvements in dietary and physical activity patterns and tobacco avoidance.

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