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## The Practice of Medicine

The Editors

## ENDURING VALUES OF THE MEDICAL PROFESSION

*No greater opportunity, responsibility, or obligation can fall to the lot of a human being than to become a physician. In the care of the suffering, [the physician] needs technical skill, scientific knowledge, and human understanding.... Tact, sympathy, and understanding are expected of the physician, for the patient is no mere collection of symptoms, signs, disordered functions, damaged organs, and disturbed emotions. [The patient] is human, fearful, and hopeful, seeking relief, help, and reassurance.*

—Harrison's Principles of Internal Medicine, 1950

The practice of medicine has changed in significant ways since the first edition of this book appeared in 1950. The advent of molecular genetics, sophisticated new imaging techniques, robotics, and advances in bioinformatics and information technology have contributed to an explosion of scientific information that has changed fundamentally the way physicians define, diagnose, treat, and attempt to prevent disease. This growth of scientific knowledge is ongoing and accelerating.

The widespread use of electronic medical records and the Internet have altered the way physicians access and exchange information as a routine part of medical practice (Fig. 1-1). As today's physicians strive to integrate copious amounts of scientific knowledge into everyday practice, it is critically important to remember two things: first, the ultimate goal of medicine is to prevent disease and, when it occurs, to diagnose it early and provide effective treatment; and second, despite nearly 70 years of scientific advances since the first edition of this text, a trusting relationship between physician and patient still lies at the heart of successful patient care.

## ■ THE SCIENCE AND ART OF MEDICINE

Deductive reasoning and applied technology form the foundation for the solution to many clinical problems. Spectacular advances in biochemistry, cell biology, and genomics, coupled with newly developed imaging techniques, allow access to the innermost parts of the cell and provide a window into the most remote recesses of the body. Revelations about the nature of genes and single cells have opened a portal for formulating a new molecular basis for the physiology of systems. Increasingly, physicians are learning how subtle changes in many different genes can affect the function of cells and organisms. Researchers are deciphering the complex mechanisms by which genes are regulated. Clinicians have developed a new appreciation of the role of stem cells in normal tissue function, in the development of cancer and other disorders, and in the treatment of certain diseases. Entirely new areas of research, including studies of chronobiology, the human microbiome, and epigenetics, have become important for understanding both health and disease. Information technology enables the interrogation of medical records from millions of individuals, yielding new insights into the etiology, characteristics, and stratification of many diseases. The knowledge gleaned from the *science of medicine* continues to enhance the understanding by physicians of complex pathologic processes and to provide new approaches to disease prevention, diagnosis, and treatment. Yet skill in the most sophisticated applications of laboratory technology and in the use of the latest therapeutic modality alone does not make a good physician.

When a patient poses challenging clinical problems, an effective physician must be able to identify the crucial elements in a complex history and physical examination; order the appropriate laboratory, imaging, and diagnostic tests; and extract the key results from densely

populated computer screens to determine whether to treat or to "watch." As the number of tests increases, so does the likelihood that some incidental finding, completely unrelated to the clinical problem at hand, will be uncovered. Deciding whether a clinical clue is worth pursuing or should be dismissed as a "red herring" and weighing whether a proposed test, preventive measure, or treatment entails a greater risk than the disease itself are essential judgments that a skilled clinician must make many times each day. This combination of medical knowledge, intuition, experience, and judgment defines the *art of medicine*, which is as necessary to the practice of medicine as is a sound scientific base.

## ■ CLINICAL SKILLS

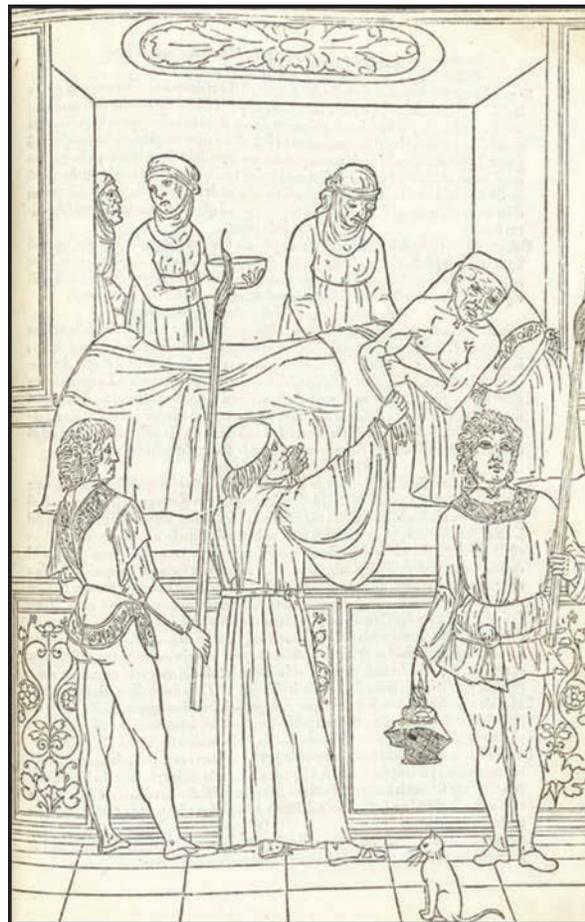
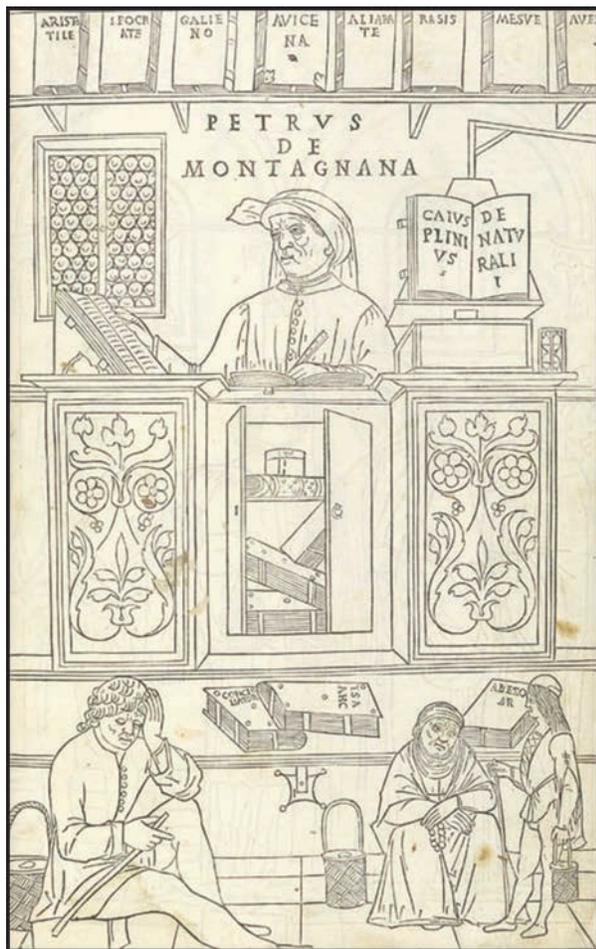
**History-Taking** The recorded history of an illness should include all the facts of medical significance in the life of the patient. Recent events should be given the most attention. Patients should, at some early point, have the opportunity to tell their own story of the illness without frequent interruption and, when appropriate, should receive expressions of interest, encouragement, and empathy from the physician. Any event related by a patient, however trivial or seemingly irrelevant, may provide the key to solving the medical problem. A methodical review of systems is important to elicit features of an underlying disease that might not be mentioned in the patient's narrative. In general, patients who feel comfortable with the physician will offer more complete information; thus, putting the patient at ease contributes substantially to obtaining an adequate history.

An informative history is more than an orderly listing of symptoms. By listening to patients and noting the way in which they describe their symptoms, physicians can gain valuable insight. Inflections of voice, facial expression, gestures, and attitude (i.e., "body language") may offer important clues to patients' perception of their symptoms. Because patients vary considerably in their medical sophistication and ability to recall facts, the reported medical history should be corroborated whenever possible. The social history also can provide important insights into the types of diseases that should be considered and can identify practical considerations for subsequent management. The family history not only identifies rare Mendelian disorders but often reveals risk factors for common disorders, such as coronary heart disease, hypertension, autoimmunity, and asthma. A thorough family history may require input from multiple relatives to ensure completeness and accuracy. An experienced clinician can usually formulate a relevant differential diagnosis from the history alone, using the physical examination and diagnostic tests to narrow the list or reveal unexpected findings that lead to more focused inquiry.

The very act of eliciting the history provides the physician with an opportunity to establish or enhance a unique bond that forms the basis for a good patient-physician relationship. This process helps the physician develop an appreciation of the patient's view of the illness, the patient's expectations of the physician and the health care system, and the financial and social implications of the illness for the patient. Although current health care settings may impose time constraints on patient visits, it is important not to rush the encounter. A hurried approach may lead patients to believe that what they are relating is not of importance to the physician, and thus they may withhold relevant information. The confidentiality of the patient-physician relationship cannot be overemphasized.

**Physical Examination** The purpose of the physical examination is to identify physical signs of disease. The significance of these objective indications of disease is enhanced when they confirm a functional or structural change already suggested by the patient's history. At times, however, physical signs may be the only evidence of disease and may not have been suggested by the history.

The physical examination should be methodical and thorough, with consideration given to the patient's comfort and modesty. Although



**FIGURE 1-1** Woodcuts from Johannes de Ketham's *Fasciculus Medicinae*, the first illustrated medical text ever printed, show methods of information access and exchange in medical practice during the early Renaissance. Initially published in 1491 for use by medical students and practitioners, *Fasciculus Medicinae* appeared in six editions over the next 25 years. *Left:* Petrus de Montagnana, a well-known physician and teacher at the University of Padua and author of an anthology of instructive case studies, consults medical texts dating from antiquity up to the early Renaissance. *Right:* A patient with plague is attended by a physician and his attendants. (Courtesy, U.S. National Library of Medicine.)

attention is often directed by the history to the diseased organ or part of the body, the examination of a new patient must extend from head to toe in an objective search for abnormalities. The results of the examination, like the details of the history, should be recorded at the time they are elicited—not hours later, when they are subject to the distortions of memory. Physical examination skills should be learned under direct observation of experienced clinicians. Even highly experienced clinicians can benefit from ongoing coaching and feedback. Simulation laboratories and standardized patients play an increasingly important role in the development of clinical skills. Although the skills of physical diagnosis are acquired with experience, it is not merely technique that determines success in identifying signs of disease. The detection of a few scattered petechiae, a faint diastolic murmur, or a small mass in the abdomen is not a question of keener eyes and ears or more sensitive fingers, but of a mind alert to those findings. Because physical findings can change with time, the physical examination should be repeated as frequently as the clinical situation warrants.

Given the many highly sensitive diagnostic tests now available (particularly imaging techniques), it may be tempting to place less emphasis on the physical examination. Indeed, many patients are seen by consultants after a series of diagnostic tests have been performed and the results are known. This fact should not deter the physician from performing a thorough physical examination since important clinical findings may have escaped detection. The act of examining (touching) the patient also offers an opportunity for communication and may have reassuring effects that foster the patient–physician relationship.

**Diagnostic Studies** Physicians rely increasingly on a wide array of laboratory and imaging tests to make diagnoses and ultimately to

solve clinical problems. However, accumulated results do not relieve the physician from the responsibility of carefully observing and examining the patient. It is also essential to appreciate the limitations of diagnostic tests. By virtue of their apparent precision, these tests often gain an aura of certainty regardless of the fallibility of the tests themselves, the instruments used in the tests, and the individuals performing or interpreting the tests. Physicians must weigh the expense involved in laboratory procedures against the value of the information these procedures are likely to provide.

Single laboratory tests are rarely ordered. Instead, physicians generally request “batteries” of multiple tests, which often prove useful and can be performed with a single specimen at relatively low cost. For example, abnormalities of hepatic function may provide the clue to nonspecific symptoms such as generalized weakness and increased fatigability, suggesting a diagnosis of chronic liver disease. Sometimes a single abnormality, such as an elevated serum calcium level, points to a particular disease, such as hyperparathyroidism or an underlying malignancy.

The thoughtful use of screening tests (e.g., measurement of low-density lipoprotein cholesterol) may allow early intervention to prevent disease (**Chap. 4**). Screening tests are most informative when they are directed toward common diseases and when their results indicate whether other useful—but often costly—tests or interventions are needed. On the one hand, biochemical measurements, together with simple laboratory determinations such as routine serum chemistries, blood counts, and urinalysis, often provide a major clue to the presence of a pathologic process. On the other hand, the physician must learn to evaluate occasional screening-test abnormalities that do not necessarily connote significant disease. An in-depth workup after the report

of an isolated laboratory abnormality in a person who is otherwise well is often wasteful and unproductive. Because so many tests are performed routinely for screening purposes, it is not unusual for one or two values to be slightly abnormal. Nevertheless, even if there is no reason to suspect an underlying illness, tests yielding abnormal results ordinarily are repeated to rule out laboratory error. If an abnormality is confirmed, it is important to consider its potential significance in the context of the patient's condition and other test results.

There is almost continual development of technically improved imaging studies with greater sensitivity and specificity. These tests provide remarkably detailed anatomic information that can be pivotal in informing medical decision-making. Ultrasonography, CT, MRI, a variety of isotopic scans, and positron emission tomography (PET) have supplanted older, more invasive approaches and opened new diagnostic vistas. In light of their capabilities and the rapidity with which they can lead to a diagnosis, it is tempting to order a battery of imaging studies. All physicians have had experiences in which imaging studies revealed findings that led to an unexpected diagnosis. Nonetheless, patients must endure each of these tests, and the added cost of unnecessary testing is substantial. Furthermore, investigation of an unexpected abnormal finding may be associated with risk and/or expense and may lead to the diagnosis of an irrelevant or incidental problem. A skilled physician must learn to use these powerful diagnostic tools judiciously, always considering whether the results will alter management and benefit the patient.

## ■ MANAGEMENT OF PATIENT CARE

**Team-Based Care** Medical practice has long involved teams, particularly physicians working with nurses. Advances in medicine have increased our ability to manage very complex clinical situations (e.g., intensive care units [ICUs], bone marrow transplantation) and have shifted the burden of disease toward chronic illnesses. Because an individual patient may have multiple chronic diseases, he or she may be cared for by different specialists as well as a primary care physician. In the inpatient setting, care may involve multiple consultants along with the primary admitting physician. Communication through the medical record is necessary but not sufficient, particularly when patients have complex medical problems or when difficult decisions need to be made about the optimal management plan. Physicians should willingly meet face-to-face or by phone to ensure clear communication and thoughtful planning. It is important to note that patients often receive or perceive different messages from various care providers; attempts should be made to provide consistency among these messages to the patient. Management plans and treatment options should be outlined succinctly and clearly for the patient.

Another dimension of team-based care involves allied health professions. It is not unusual for a hospitalized patient to encounter physical therapists, pharmacists, respiratory therapists, radiology technicians, social workers, dietitians, and transport personnel (among others) in addition to physicians and nurses. Each of these individuals contributes to clinical care as well as to the patient's experience with the health care system. In the outpatient setting, disease screening and chronic disease management are often carried out by nurses, physician assistants, or other allied health professionals.

The growth of team-based care has important implications for medical culture, student and resident training, and the organization of health care systems. Despite diversity in training, skills, and responsibilities among health care professionals, common values need to be espoused and reinforced. Many medical schools have incorporated interprofessional teamwork into their curricula. Effective communication is inevitably the most challenging aspect of implementing team-based care. While communication can be aided by electronic devices, including medical records, apps, or text messages, it is vitally important to balance efficiency with taking the necessary time to speak directly with colleagues.

**The Dichotomy of Inpatient and Outpatient Internal Medicine** The hospital environment has experienced sweeping changes over the last few decades. Emergency departments and critical

care units have evolved to manage critically ill patients, allowing them to survive formerly fatal conditions. In parallel, there is increasing pressure to reduce the length of stay in the hospital and to manage complex disorders in the outpatient setting. This transition has been driven not only by efforts to reduce costs but also by the availability of new outpatient technologies, such as imaging and percutaneous infusion catheters for long-term antibiotics or nutrition, minimally invasive surgical procedures, and evidence that outcomes often are improved by reducing inpatient hospitalization.

In addition to traditional medical beds, hospitals now encompass multiple distinct levels of care, such as the emergency department, procedure rooms, overnight observation units, critical care units, and palliative care units. A consequence of this differentiation has been the emergence of new specialties (e.g., emergency medicine and end-of-life care) and the provision of in-hospital care by hospitalists and intensivists. Most *hospitalists* are board-certified internists who bear primary responsibility for the care of hospitalized patients and whose work is limited entirely to the hospital setting. The shortened length of hospital stay means that most patients receive only acute care while hospitalized; the increased complexities of inpatient medicine make the presence of an internist with specific training, skills, and experience in the hospital environment extremely beneficial. *Intensivists* are board-certified physicians who are further certified in critical care medicine and who direct and provide care for very ill patients in critical care units. Clearly, an important challenge in internal medicine today is to ensure the continuity of communication and information flow between a patient's primary care physician and those who are in charge of the patient's hospital care. Maintaining these channels of communication is frequently complicated by patient "handoffs"—i.e., transitions from the outpatient to the inpatient environment, from the critical care unit to a general medicine floor, from a medical to a surgical service and vice versa, and from the hospital to the outpatient environment.

The involvement of many care providers in conjunction with these transitions can threaten the traditional one-to-one relationship between patient and primary care physician. Of course, patients can benefit greatly from effective collaboration among a number of health care professionals; however, *it is the duty of the patient's principal or primary physician to provide cohesive guidance through an illness*. To meet this challenge, primary care physicians must be familiar with the techniques, skills, and objectives of specialist physicians and allied health professionals who care for their patients in the hospital. In addition, primary care physicians must ensure that their patients benefit from scientific advances and the expertise of specialists, both in and out of the hospital. Primary care physicians should explain the role of these specialists to reassure patients that they are in the hands of physicians best trained to manage an acute illness. However, the primary care physician should assure patients and their families that decisions are being made in consultation with these specialists. The evolving concept of the "medical home" incorporates team-based primary care with subspecialty care in a cohesive environment that ensures smooth transitions of care.

**Mitigating the Stress of Acute Illness** Few people are prepared for a new diagnosis of cancer or anticipate the occurrence of a myocardial infarction, stroke, or major accident. The care of a frightened or distraught patient is confounded by these understandable responses to life-threatening events. The physician and other health providers can reduce the shock of life-changing events by providing information in a clear, calm, consistent, and reassuring manner. Often, information and reassurance need to be repeated. Caregivers should also recognize that, for outsiders, hospital emergency rooms, operating rooms, ICUs, and general medical floors represent an intimidating environment. Hospitalized patients find themselves surrounded by air jets, buttons, and glaring lights; invaded by tubes and wires; and beset by the numerous members of the health care team—hospitalists, specialists, nurses, nurses' aides, physicians' assistants, social workers, technologists, physical therapists, medical students, house officers, attending and consulting physicians, and many others. They may be

transported to special laboratories and imaging facilities replete with blinking lights, strange sounds, and unfamiliar personnel; they may be left unattended at times; and they may be obligated to share a room with other patients who have their own health problems. It is little wonder that patients may be stressed by this environment. Physicians who appreciate the hospital experience from the patient's perspective and who make an effort to guide the patient through this experience may make a stressful situation more tolerable and enhance the patient's chances for an optimal recovery.

**Medical Decision-Making** Medical decision-making is a fundamental responsibility of the physician and occurs at each stage of the diagnostic and therapeutic process. The decision-making process involves the ordering of additional tests, requests for consultations, decisions about treatment, and predictions concerning prognosis. This process requires an in-depth understanding of the pathophysiology and natural history of disease. Formulating a differential diagnosis requires not only a broad knowledge base but also the ability to assess the relative probabilities of various diseases for a given patient. Application of the scientific method, including hypothesis formulation and data collection, is essential to the process of accepting or rejecting a particular diagnosis. Analysis of the differential diagnosis is an iterative process. As new information or test results are acquired, the group of disease processes being considered can be contracted or expanded appropriately. Whenever possible, decisions should be evidence-based, taking advantage of rigorously designed clinical trials or objective comparisons of different diagnostic tests. *Evidence-based medicine* is in sharp contrast to anecdotal experience, which is often biased. Unless attuned to the importance of using larger, objective studies for making decisions, even the most experienced physicians can be influenced to an undue extent by recent encounters with selected patients. Evidence-based medicine has become an increasingly important part of routine medical practice and has led to the publication of many useful practice guidelines.

Despite the importance of evidence-based medicine, much medical decision-making still relies on good clinical judgment, an attribute that is difficult to quantify or even to assess qualitatively. Physicians must use their knowledge and experience as a basis for weighing known factors, along with the inevitable uncertainties, and then making a sound judgment; this synthesis of information is particularly important when a relevant evidence base is not available. Several quantitative tools may be invaluable in synthesizing the available information, including diagnostic tests, Bayes' theorem, and multivariate statistical models. Diagnostic tests serve to reduce uncertainty about an individual's diagnosis or prognosis and help the physician decide how best to manage that individual's condition. The battery of diagnostic tests complements the history and the physical examination. The accuracy of a particular test is ascertained by determining its sensitivity (true-positive rate) and specificity (true-negative rate) as well as the predictive value of a positive and a negative result. [See Chap. 3 for a more thorough discussion of decision-making in clinical medicine.](#)

**Practice Guidelines** Many professional organizations and government agencies have developed formal clinical-practice guidelines to aid physicians and other caregivers in making diagnostic and therapeutic decisions that are evidence-based, cost-effective, and most appropriate to a particular patient and clinical situation. As the evidence base of medicine increases, guidelines can provide a useful framework for managing patients with particular diagnoses or symptoms. Clinical guidelines can protect patients—particularly those with inadequate health care benefits—from receiving substandard care. These guidelines also can protect conscientious caregivers from inappropriate charges of malpractice and society from the excessive costs associated with the overuse of medical resources. There are, however, caveats associated with clinical-practice guidelines since they tend to oversimplify the complexities of medicine. Furthermore, groups with different perspectives may develop divergent recommendations regarding issues as basic as the need for screening of women

by mammography or of men by serum prostate-specific antigen (PSA). Finally, guidelines, as the term implies, do not—and cannot be expected to—account for the uniqueness of each individual and his or her illness. The physician's challenge is to integrate into clinical practice the useful recommendations offered by experts without accepting them blindly or being inappropriately constrained by them.

**Precision Medicine** The concept of *precision* or *personalized medicine* reflects the growing recognition that diseases once lumped together can be further stratified on the basis of genetic, biomarker, phenotypic, and/or psychosocial characteristics that distinguish a given patient from other patients with similar clinical presentations. Inherent in this concept is the goal of targeting therapies in a more specific way to improve clinical outcomes for the individual patient and minimize unnecessary side effects for those less likely to respond to a particular treatment. In some respects, precision medicine represents the evolution of clinical practice guidelines, which are usually developed for populations of patients or a particular diagnosis (e.g., hypertension, thyroid nodule). As the pathophysiology, prognosis, and treatment responses of subgroups within these diagnoses become better understood, the relevant clinical guidelines incorporate progressively more refined recommendations for individuals within these subgroups. The role of precision medicine is particularly important for cancers in which genetic testing is able to predict responses (or the lack thereof) to targeted therapies ([Chap. 69](#)). One can anticipate similar applications of precision medicine in pharmacogenomics, immunologic disorders, and diseases in which biomarkers better predict treatment responses.

**Evaluation of Outcomes** Clinicians generally use *objective* and readily measurable parameters to judge the outcome of a therapeutic intervention. These measures may oversimplify the complexity of a clinical condition as patients often present with a major clinical problem in the context of multiple complicating background illnesses. For example, a patient may present with chest pain and cardiac ischemia, but with a background of chronic obstructive pulmonary disease and renal insufficiency. For this reason, outcome measures such as mortality, length of hospital stay, or readmission rates are typically risk-adjusted. An important point to remember is that patients usually seek medical attention for *subjective* reasons; they wish to obtain relief from pain, to preserve or regain function, and to enjoy life. The components of a patient's health status or quality of life can include bodily comfort, capacity for physical activity, personal and professional function, sexual function, cognitive function, and overall perception of health. Each of these important domains can be assessed through structured interviews or specially designed questionnaires. Such assessments provide useful parameters by which a physician can judge patients' subjective views of their disabilities and responses to treatment, particularly in chronic illness. The practice of medicine requires consideration and integration of both objective and subjective outcomes.

Many health systems use survey and patient feedback data to assess qualitative features such as patient satisfaction, access to care, and communication with nurses and physicians. In the United States, HCAHPS (Hospital Consumer Assessment of Healthcare Providers and Systems) surveys are used by many systems and are publically reported. Social media is also being used to assess feedback in real time as well as to share patient experiences with health care systems.

**Errors in the Delivery of Health Care** A series of reports from the Institute of Medicine (now the National Academy of Medicine [NAM]) called for an ambitious agenda to reduce medical error rates and improve patient safety by designing and implementing fundamental changes in health care systems. It is the responsibility of hospitals and health care organizations to develop systems to reduce risk and ensure patient safety. Medication errors can be reduced through the use of ordering systems that rely on electronic processes or, when electronic options are not available, that eliminate misreading of handwriting. Whatever the clinical situation, it is the physician's responsibility to use powerful therapeutic measures wisely, with due regard for their beneficial actions, potential dangers, and cost. Implementation of infection

control systems, enforcement of hand-washing protocols, and careful oversight of antibiotic use can minimize the complications of nosocomial infections. Central-line infection rates have been dramatically reduced at many centers by careful adherence of trained personnel to standardized protocols for introducing and maintaining central lines. Rates of surgical infection and wrong-site surgery can likewise be reduced by the use of standardized protocols and checklists. Falls by patients can be minimized by judicious use of sedatives and appropriate assistance with bed-to-chair and bed-to-bathroom transitions. Taken together, these and other measures are saving thousands of lives each year.

**Electronic Medical Records** Both the growing reliance on computers and the strength of information technology now play central roles in medicine, including efforts to reduce medical errors. Laboratory data are accessed almost universally through computers. Many medical centers now have electronic medical records (EMRs), computerized order entry, and bar-coded tracking of medications. Some of these systems are interactive, sending reminders or warning of potential medical errors.

EMRs offer rapid access to information that is invaluable in enhancing health care quality and patient safety, including relevant data, historical and clinical information, imaging studies, laboratory results, and medication records. These data can be used to monitor and reduce unnecessary variations in care and to provide real-time information about processes of care and clinical outcomes. Ideally, patient records are easily transferred across the health care system. However, technological limitations and concerns about privacy and cost continue to limit broad-based use of EMRs in many clinical settings.

For all of the advantages of EMRs, they can create distance between the physician and patient if care is not taken to preserve face-to-face contact. EMRs also require training and time for data entry. Many providers spend significant time entering information to generate structured data and to meet billing requirements. They may feel pressured to take short cuts, such as “cutting and pasting” parts of earlier notes into the daily record, thereby increasing the risk of errors. EMRs also structure information in a manner that disrupts the traditional narrative flow across time and among providers. These features, which may be frustrating for some providers, must be weighed against the advantages of ready access to past medical history, imaging, laboratory data, and consultant notes.

It is important to emphasize that information technology is merely a tool and can never replace the clinical decisions that are best made by the physician. Clinical knowledge and an understanding of a patient’s needs, supplemented by quantitative tools, still represent the best approach to decision-making in the practice of medicine.

## THE PATIENT–PHYSICIAN RELATIONSHIP

*The significance of the intimate personal relationship between physician and patient cannot be too strongly emphasized, for in an extraordinarily large number of cases both the diagnosis and treatment are directly dependent on it. One of the essential qualities of the clinician is interest in humanity, for the secret of the care of the patient is in caring for the patient.*

—Francis W. Peabody, October 21, 1925,  
Lecture at Harvard Medical School

Physicians must never forget that patients are individuals with problems that all too often transcend their physical complaints. They are not “cases” or “admissions” or “diseases.” Patients do not fail treatments; treatments fail to benefit patients. This point is particularly important in this era of high technology in clinical medicine. Most patients are anxious and fearful. Physicians should instill confidence and offer reassurance, but they must never come across as arrogant or patronizing. A professional attitude, coupled with warmth and openness, can do much to alleviate anxiety and to encourage patients to share all aspects of their medical history. Empathy and compassion are the essential features of a caring physician. The physician needs to consider the setting in which an illness occurs—in terms not only of patients themselves

but also of their familial, social, and cultural backgrounds. The ideal patient–physician relationship is based on thorough knowledge of the patient, mutual trust, and the ability to communicate.

**Informed Consent** The fundamental principles of medical ethics require physicians to act in the patient’s best interest and to respect the patient’s autonomy. These requirements are particularly relevant to the issue of informed consent. Patients are required to sign consent forms for most diagnostic or therapeutic procedures. Many patients possess limited medical knowledge and must rely on their physicians for advice. Communicating in a clear and understandable manner, physicians must fully discuss the alternatives for care and explain the risks, benefits, and likely consequences of each alternative. The physician is responsible for ensuring that the patient thoroughly understands these risks and benefits; encouraging questions is an important part of this process. It may be necessary to go over certain issues with the patient more than once. This is the very definition of *informed consent*. Complete, clear explanation and discussion of the proposed procedures and treatment can greatly mitigate the fear of the unknown that commonly accompanies hospitalization. Often the patient’s understanding is enhanced by repeatedly discussing the issues in an unthreatening and supportive way, answering new questions that occur to the patient as they arise. Clear communication can also help alleviate misunderstandings in situations where complications of intervention occur.

Special care should be taken to ensure that a physician seeking a patient’s informed consent has no real or apparent conflict of interest.

**Approach to Grave Prognoses and Death** No circumstance is more distressing than the diagnosis of an incurable disease, particularly when premature death is inevitable. What should the patient and family be told? What measures should be taken to maintain life? What can be done to optimize quality of life?

Transparency of information, delivered in an appropriate manner, is essential in the face of a terminal illness. Even patients who seem unaware of their medical circumstances, or whose family members have protected them from diagnoses or prognoses, often have keen insights into their condition. They may also have misunderstandings that can lead to additional anxiety. The patient must be given an opportunity to talk with the physician and ask questions. A wise and insightful physician uses such open communication as the basis for assessing what the patient wants to know and when he or she wants to know it. On the basis of the patient’s responses, the physician can assess the right tempo for sharing information. Ultimately, the patient must understand the expected course of the disease so that appropriate plans and preparations can be made. The patient should participate in decision-making with an understanding of the goal of treatment (palliation) and its likely effects. The patient’s religious beliefs should be taken into consideration. Some patients may find it easier to share their feelings about death with their physician, nurses, or members of the clergy than with family members or friends.

The physician should provide or arrange for emotional, physical, and spiritual support and must be compassionate, unhurried, and open. In many instances, there is much to be gained by the laying on of hands. Pain should be controlled adequately, human dignity maintained, and isolation from family and close friends avoided. These aspects of care tend to be overlooked in hospitals, where the intrusion of life-sustaining equipment can detract from attention to the whole person and encourage concentration instead on the life-threatening disease, against which the battle ultimately will be lost in any case. In the face of terminal illness, the goal of medicine must shift from *cure* to *care* in the broadest sense of the term. *Primum succurrere*, first hasten to help, is a guiding principle. In offering care to a dying patient, a physician should be prepared to provide information to family members and deal with their grief and sometimes their feelings of guilt or even anger. It is important for the physician to assure the family that everything reasonable is being done. A substantial challenge in these discussions is that the physician often does not know how to gauge the prognosis. In addition, various members of the health care team may offer different opinions. Good communication among providers is

essential so that consistent information is provided to patients. This is especially important when the best path forward is uncertain. Advice from experts in palliative and terminal care should be sought whenever appropriate to ensure that clinicians are not providing patients with unrealistic expectations. [For a more complete discussion of end-of-life care, see Chap. 9.](#)

**Maintaining Humanism and Professionalism** Many trends in the delivery of health care tend to make medical care impersonal. These trends, some of which have been mentioned already, include (1) vigorous efforts to reduce the escalating costs of health care; (2) the growing number of managed-care programs, which are intended to reduce costs but in which the patient may have little choice in selecting a physician; (3) increasing reliance on technological advances and computerization; and (4) the need for numerous physicians and other health professionals to be involved in the care of most patients who are seriously ill.

In light of these changes in the medical care system, it is a major challenge for physicians to maintain the *humane* aspects of medical care. The American Board of Internal Medicine, working together with the American College of Physicians–American Society of Internal Medicine and the European Federation of Internal Medicine, has published a *Charter on Medical Professionalism* that underscores three main principles in physicians' contract with society: (1) the primacy of patient welfare, (2) patient autonomy, and (3) social justice. While medical schools appropriately place substantial emphasis on professionalism, a physician's personal attributes, including integrity, respect, and compassion, also are extremely important. In the United States, the Gold Humanism Society recognizes individuals who are exemplars of humanistic patient care and serve as role models for medical education and training.

Availability to the patient, expression of sincere concern, willingness to take the time to explain all aspects of the illness, and a nonjudgmental attitude when dealing with patients whose cultures, lifestyles, attitudes, and values differ from those of the physician are just a few of the characteristics of a humane physician. Every physician will, at times, be challenged by patients who evoke strongly negative or positive emotional responses. Physicians should be alert to their own reactions to such situations and should consciously monitor and control their behavior so that the patient's best interest remains the principal motivation for their actions at all times.

Another important aspect of patient care involves an appreciation of the patient's "quality of life," a subjective assessment of what each patient values most. This assessment requires detailed, sometimes intimate knowledge of the patient, which usually can be obtained only through deliberate, unhurried, and often repeated conversations. Time pressures will always threaten these interactions, but they should not diminish the importance of understanding and seeking to fulfill the priorities of the patient.

## ■ EXPANDING FRONTIERS IN MEDICAL PRACTICE

**The Era of "Omics"** In the spring of 2003, announcement of the complete sequencing of the human genome officially ushered in the genomic era. However, even before that landmark accomplishment, the practice of medicine had been evolving as a result of insights into both the human genome and the genomes of a wide variety of microbes. The clinical implications of these insights are illustrated by the complete genome sequencing of H1N1 influenza virus in 2009 and the rapid identification of H1N1 influenza as a potentially fatal pandemic illness, leading to the swift development and dissemination of an effective protective vaccine. Today, gene expression profiles are being used to guide therapy and inform prognosis for a number of diseases, and genotyping is providing a new means to assess the risk of certain diseases as well as variations in response to a number of drugs. Despite these advances, the use of complex genomics in the diagnosis, prevention, and treatment of disease is still in its early stages. The task of physicians is complicated by the fact that phenotypes generally are determined not by genes alone but by the interplay of genetic and environmental factors.

Rapid progress is also being made in other areas of molecular medicine. *Epigenetics* is the study of alterations in chromatin and histone proteins and methylation of DNA sequences that influence gene expression ([Chap. 471](#)). Every cell of the body has identical DNA sequences; the diverse phenotypes a person's cells manifest are the result of epigenetic regulation of gene expression. Epigenetic alterations are associated with a number of cancers and other diseases. *Proteomics*, the study of the entire library of proteins made in a cell or organ and the complex relationship of these proteins to disease, is enhancing the repertoire of the 23,000 genes in the human genome through alternate splicing, posttranslational processing, and posttranslational modifications that often have unique functional consequences. The presence or absence of particular proteins in the circulation or in cells is being explored for diagnostic and disease-screening applications. *Microbiomics* is the study of the resident microbes in humans and other mammals, which together compose the microbiome. The human haploid genome has ~23,000 genes, whereas the microbes residing on and in the human body encompass more than 3–4 million genes; these resident microbes are likely to be of great significance with regard to health status. Ongoing research is demonstrating that the microbes inhabiting human mucosal and skin surfaces play a critical role in maturation of the immune system, in metabolic balance, and in disease susceptibility. A variety of environmental factors, including the use and overuse of antibiotics, have been tied experimentally to substantial increases in disorders such as obesity, metabolic syndrome, atherosclerosis, and immune-mediated diseases in both adults and children. *Metagenomics*, of which microbiomics is a part, is the genomic study of environmental species that have the potential to influence human biology directly or indirectly. An example is the study of exposures to microorganisms in farm environments that may be responsible for the lower incidence of asthma among children raised on farms. *Metabolomics* is the study of the range of metabolites in cells or organs and the ways they are altered in disease states. The aging process itself may leave telltale metabolic footprints that allow the prediction (and possibly the prevention) of organ dysfunction and disease. It seems likely that disease-associated patterns will be found in lipids, carbohydrates, membranes, mitochondria, and other vital components of cells and tissues. *Exposomics* is the study of the exposome—i.e., the environmental exposures such as smoking, sunlight, diet, exercise, education, and violence that together have an enormous impact on health. All of this new information represents a challenge to the traditional reductionist approach to medical thinking. The variability of results in different patients, together with the large number of variables that can be assessed, creates challenges in identifying preclinical disease and defining disease states unequivocally. Accordingly, the tools of *systems biology* and *network medicine* are being applied to the enormous body of information now obtainable for every patient and may eventually provide new approaches to classifying disease. [For a more complete discussion of a complex systems approach to human disease, see Chap. 476.](#)

The rapidity of these advances may seem overwhelming to practicing physicians. However, physicians have an important role to play in ensuring that these powerful technologies and sources of new information are applied judiciously to patient care. Since "omics" are evolving so rapidly, physicians and other health care professionals must engage in continuous learning so that they can apply this new knowledge to the benefit of their patients' health and well-being. Genetic testing requires wise counsel based on an understanding of the value and limitations of the tests as well as the implications of their results for specific individuals. [For a more complete discussion of genetic testing, see Chap. 457.](#)

**The Globalization of Medicine** Physicians should be cognizant of diseases and health care services beyond local boundaries. Global travel has implications for disease spread, and it is not uncommon for diseases endemic to certain regions to be seen in other regions after a patient has traveled to and returned from those regions. The outbreak of Zika virus infections in the Americas is a cogent example of this phenomenon. In addition, factors such as wars, the migration of refugees, and climate change are contributing to changing disease

profiles worldwide. Patients have broader access to unique expertise or clinical trials at distant medical centers, and the cost of travel may be offset by the quality of care at those distant locations. As much as any other factor influencing global aspects of medicine, the Internet has transformed the transfer of medical information throughout the world. This change has been accompanied by the transfer of technological skills through telemedicine and international consultation—for example, interpretation of radiologic images and pathologic specimens. **For a complete discussion of global issues, see Chap. 460.**

**Medicine on the Internet** On the whole, the Internet has had a positive effect on the practice of medicine; through personal computers, a wide range of information is available to physicians and patients almost instantaneously at any time and from anywhere in the world. This medium holds enormous potential for the delivery of current information, practice guidelines, state-of-the-art conferences, journal content, textbooks (including this text), and direct communications with other physicians and specialists, expanding the depth and breadth of information available to the physician regarding the diagnosis and care of patients. Medical journals are now accessible online, providing rapid sources of new information. By bringing them into direct and timely contact with the latest developments in medical care, this medium also serves to lessen the information gap that has hampered physicians and health care providers in remote areas.

Patients, too, are turning to the Internet in increasing numbers to acquire information about their illnesses and therapies and to join Internet-based support groups. Patients often arrive at a clinic visit with sophisticated information about their illnesses. In this regard, physicians are challenged in a positive way to keep abreast of the latest relevant information while serving as an “editor” as patients navigate this seemingly endless source of information, the accuracy and validity of which are not uniform.

A critically important caveat is that virtually anything can be published on the Internet, with easy circumvention of the peer-review process that is an essential feature of academic publications. Both physicians and patients who search the Internet for medical information must be aware of this danger. Notwithstanding this limitation, appropriate use of the Internet is revolutionizing information access for physicians and patients and in this regard represents a remarkable resource that was not available to practitioners a generation ago.

**Public Expectations and Accountability** The general public’s level of knowledge and sophistication regarding health issues has grown rapidly over the last few decades. As a result, expectations of the health care system in general and of physicians in particular have risen. Physicians are expected to master rapidly advancing fields (the *science* of medicine) while considering their patients’ unique needs (the *art* of medicine). Thus, physicians are held accountable not only for the technical aspects of the care they provide but also for their patients’ satisfaction with the delivery and costs of care.

In many parts of the world, physicians increasingly are expected to account for the way in which they practice medicine by meeting certain standards prescribed by federal and local governments. The hospitalization of patients whose health care costs are reimbursed by the government and other third parties is subjected to utilization review. Thus, a physician must defend the cause for and duration of a patient’s hospitalization if it falls outside certain “average” standards. Authorization for reimbursement increasingly is based on documentation of the nature and complexity of an illness, as reflected by recorded elements of the history and physical examination. A growing “pay-for-performance” movement seeks to link reimbursement to quality of care. The goal of this movement is to improve standards of health care and contain spiraling health care costs. In many parts of the United States, managed (capitated) care contracts with insurers have replaced traditional fee-for-service care, placing the onus of managing the cost of all care directly on the providers and increasing the emphasis on preventive strategies. In addition, physicians are expected to give evidence of their current competence through mandatory continuing education, patient record audits, maintenance of certification, and relicensing.

**Medical Ethics and New Technologies** The rapid pace of technological advances has profound implications for medical applications that go far beyond the traditional goals of disease prevention, treatment, and cure. Cloning, genetic engineering, gene therapy, human-computer interfaces, nanotechnology, and use of targeted therapies have the potential to modify inherited predispositions to disease, select desired characteristics in embryos, augment “normal” human performance, replace failing tissues, and substantially prolong life span. Given their unique training, physicians have a responsibility to help shape the debate on the appropriate uses of and limits placed on these new techniques and to consider carefully the ethical issues associated with the implementation of such interventions. As medicine becomes more complex, shared decision-making is increasingly important, particularly in areas such as genetic counseling and end-of-life care, but also in most instances of considering diagnostic and treatment options.

**Learning Medicine** More than a century has passed since the publication of the Flexner Report, a seminal study that transformed medical education and emphasized the scientific foundations of medicine as well as the acquisition of clinical skills. In an era of burgeoning information and access to medical simulation and informatics, many schools are implementing new curricula that emphasize lifelong learning and the acquisition of competencies in teamwork, communication skills, system-based practice, and professionalism. The tools of medicine also change continuously, necessitating formal training in the use of EMRs, large datasets, ultrasound, robotics, and new imaging techniques. These and other features of the medical school curriculum provide the foundation for many of the themes highlighted in this chapter and are expected to allow physicians to progress, with experience and learning over time, from competency to proficiency to mastery.

At a time when the amount of information that must be mastered to practice medicine continues to expand, increasing pressures both within and outside of medicine have led to the implementation of restrictions on the amount of time a physician-in-training can spend in the hospital and in clinics. Because the benefits associated with continuity of medical care and observation of a patient’s progress over time were thought to be outstripped by the stresses imposed on trainees by long hours and by fatigue-related errors, strict limits were set on the number of patients that trainees could be responsible for at one time, the number of new patients they could evaluate in a day on call, and the number of hours they could spend in the hospital. In 1980, residents in medicine worked in the hospital more than 90 hours per week on average. In 1989, their hours were restricted to no more than 80 per week. Resident physicians’ hours further decreased by ~10% between 1996 and 2008, and in 2010 the Accreditation Council for Graduate Medical Education further restricted (i.e., to 16 hours per shift) consecutive in-hospital duty hours for first-year residents. The impact of these changes is still being assessed, but the evidence that medical errors have decreased as a consequence is sparse. An unavoidable by-product of fewer hours at the bedside is an increase in the number of “handoffs” of patient responsibility from one physician to another. These transfers often involve a transition from a physician who knows the patient well, having evaluated that individual on admission, to a physician who knows the patient less well. It is imperative that these transitions of responsibility be handled with care and thoroughness, with all relevant information exchanged and acknowledged.

**The Physician as Perpetual Student** From the time physicians graduate from medical school, it becomes all too apparent that this milestone is symbolic and that they must embrace the role of a “perpetual student.” This realization is at the same time exhilarating and anxiety-provoking. It is exhilarating because physicians can apply constantly expanding knowledge to the treatment of their patients; it is anxiety-provoking because physicians realize that they will never know as much as they want or need to know. Ideally, physicians will translate the latter feeling into energy through which they can continue to improve and reach their potential. It is the physician’s responsibility to pursue new knowledge continually by reading, attending

conferences and courses, and consulting colleagues and the Internet. This is often a difficult task for a busy practitioner; however, a commitment to continued learning is an integral part of being a physician and must be given the highest priority.

**The Physician as Citizen** Being a physician is a privilege. The capacity to apply one's skills for the benefit of fellow human beings is a noble calling. The physician–patient relationship is inherently unbalanced in the distribution of power. In light of their influence, physicians must always be aware of the potential impact of what they do and say and must always strive to strip away individual biases and preferences to find what is best for their patients. To the extent possible, physicians should also act within their communities to promote health and alleviate suffering. Meeting these goals begins by setting a healthy example and continues in taking action to deliver needed care even when personal financial compensation may not be available.

**Research, Teaching, and the Practice of Medicine** The word *doctor* is derived from the Latin *docere*, “to teach.” As teachers, physicians should share information and medical knowledge with colleagues, students of medicine and related professions, and their patients. The practice of medicine is dependent on the sum total of medical knowledge, which in turn is based on an unending chain of scientific discovery, clinical observation, analysis, and interpretation. Advances in medicine depend on the acquisition of new information through research, and improved medical care requires the transmission of that information. As part of their broader societal responsibilities, physicians should encourage patients to participate in ethical and properly approved clinical investigations if these studies do not impose undue hazard, discomfort, or inconvenience. Physicians engaged in clinical research must be alert to potential conflicts of interest between their research goals and their obligations to individual patients. The best interests of the patient must always take priority.

*To wrest from nature the secrets which have perplexed philosophers in all ages, to track to their sources the causes of disease, to correlate the vast stores of knowledge, that they may be quickly available for the prevention and cure of disease—these are our ambitions.*

—William Osler, 1849–1919

### ■ FURTHER READING

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## 2

## Promoting Good Health

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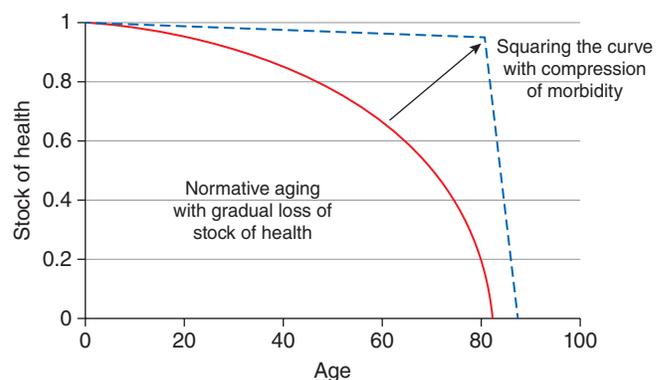


### ■ GOALS AND APPROACHES TO PREVENTION

Prevention of acute and chronic diseases before their onset has been recognized as one of the hallmarks of excellent medical practice for centuries, and is now used as a metric for highly functioning health-care systems. The ultimate goal of preventive strategies is to avoid premature death. However, as longevity has increased dramatically worldwide over the last century (largely as a result of public health practices), increasing emphasis is placed on prevention for the purpose of preserving quality of life and extending the healthspan, not just the lifespan. Given that all patients will eventually die, the goal of prevention ultimately becomes compression of morbidity toward the end of the lifespan; that is, reduction of the amount of burden and time spent with disease prior to dying. As shown in Fig. 2-1, normative aging tends to involve a steady decline in the stock of health, with accelerating decline over time. Successful prevention offers the opportunity both to extend life and to extend healthy life, thus “squaring the curve” of health loss during aging.

Prevention strategies have been characterized as tertiary, secondary, primary, and primordial. *Tertiary prevention* requires rapid action to prevent imminent death in the setting of acute illness, such as through percutaneous coronary intervention in the setting of ST-segment elevation myocardial infarction. *Secondary prevention* strategies focus on avoiding the recurrence of disease and death in an individual who is already affected. For example, tamoxifen is recommended for women with surgically treated early-stage, estrogen-receptor-positive breast cancer, because it reduces the risk of recurrent breast cancer (including in the contralateral breast) and death. *Primary prevention* attempts to reduce the risk of incident disease among individuals with a risk factor. Treatment of elevated blood pressure in individuals who have not yet experienced cardiovascular disease represents one example of primary prevention that has proven effective in reducing the incidence of stroke, heart failure, and coronary heart disease.

*Primordial prevention* is a more recent concept (first introduced in 1979) which focuses on prevention of the development of *risk factors* for disease, not just prevention of disease. Primordial prevention strategies emphasize upstream determinants of risk for chronic diseases, such as eating patterns, physical activity, and environmental and social determinants of health. It therefore encompasses medical treatment strategies for individuals as well as a strong reliance on public health and social policy. It is increasingly clear that primordial prevention represents the ultimate means for reducing the burden of chronic diseases of aging. Once risk factors develop, it is difficult



**FIGURE 2-1 Loss of health with aging.** Representation of normative aging with loss of the full stock of health with which individuals are born (indicating gain of morbidity), contrasted with a squared curve with greater longevity and fuller stock of health (less morbidity) until shortly before death. The “squared curve” represents the likely ideal situation for most patients.

to restore risk to the low level of someone who never developed the risk factor. The time spent with adverse levels of the risk factor often causes irreversible damage that precludes complete restoration of low risk. For example, individuals with hypertension who are treated back to optimal levels (<120/<80 mmHg) do have a lower risk compared with untreated patients with hypertension, but they still have twice the risk of cardiovascular events as those who maintained optimal blood pressure without medications. Patients with elevated blood pressure that is subsequently treated have greater left ventricular mass index, worse renal function, and more evidence of atherosclerosis and other target organ damage as a result of the time spent with elevated blood pressure; such damage cannot be fully reversed despite efficacious therapy with antihypertensive medications. Conversely, as described below in greater detail, individuals who maintain optimal levels of all major cardiovascular risk factors into middle age through primordial prevention essentially abolish their lifetime risk of developing cardiovascular disease while also living substantially longer and having a lower burden of other comorbid illnesses (compression of morbidity).

Prevention strategies should be distinguished from disease screening strategies. Screening attempts to detect evidence of disease at its earliest stages, when treatment is likely to be more efficacious than for advanced disease (Chap. 4). Screening can be performed in service of prevention, especially if it aids in identifying pre-clinical markers associated with elevated disease risk.

### ■ HEALTH PROMOTION

In recent decades, medical practice has increasingly focused on public health approaches to promote health, and not just prevent disease. Prevention of disease is a worthy individual and societal goal in and of itself, but it does not necessarily guarantee health. Health is a broader construct encompassing more than just absence of disease. It includes biological, physiological, and psychological domains (among others) in a continuum, rather than occurring as a dichotomous trait. Health is therefore somewhat subjective, but attempts have been made to use more objective criteria to define health in order to raise awareness, prevent disease, and promote healthy longevity.

For example, in 2010 the American Heart Association (AHA) defined a new construct of “cardiovascular health” based on evidence of associations with longevity, disease avoidance, healthy longevity, and quality of life. The definition of cardiovascular health is based on seven health behaviors and health factors (eating pattern, physical activity, body mass, smoking status, and levels of blood pressure, blood cholesterol, and blood glucose) and includes a spectrum from poor to ideal. Individuals with optimal levels of all seven metrics simultaneously are considered to have ideal cardiovascular health. The state of cardiovascular health for an individual or a population can be assessed with simple scoring by counting the number of ideal metrics (out of 7) or applying 0 points for each poor metric, 1 point for each intermediate metric, and 2 points for each ideal metric, thus creating a composite cardiovascular health score ranging from 0 to 14 points. Higher cardiovascular health scores in younger and middle ages have been associated with greater longevity, lower incidence of cardiovascular disease, lower incidence of other chronic diseases of aging (including dementia, cancer, and more), compression of morbidity, greater quality of life, and lower healthcare costs, achieving both individual and societal goals for healthy aging, and further establishing the critical importance of primordial prevention and cardiovascular health promotion.

Focusing on health promotion, rather than just disease prevention, may also provide greater motivation for patients to pursue lifestyle changes or adhere to clinician recommendations. Extensive literature suggests that providing patients solely with information regarding disease risk, or risk reduction with treatment, is unlikely to motivate desired behavior change. Empowering patients with strategies to achieve positive health goals after discussing risks can provide more effective adherence and better long-term outcomes. In the case of smoking cessation, enumerating only the risks of smoking can lead to patient inertia and therapeutic nihilism, and has proven an ineffective approach, whereas strategies that incorporate positive

health messaging, support and feedback, with appropriate use of evidence-based therapies, have proven far more effective.

### ■ PRIORITIZING PREVENTION STRATEGIES

In secondary prevention, the patient already has manifest clinical disease, and is therefore at high risk for progression. The approach should be to work with the patient to implement all evidence-based strategies that will help to prevent recurrence or progression. This will typically include drug therapy as well as therapeutic lifestyle changes to control ongoing risk factors which may have caused disease in the first place. Juggling priorities can be difficult, and barriers to implementation are many, including costs, time, patient health literacy, and patient and caregiver capacity to organize the regimen. Addressing these potential barriers with the patient can help to forge a therapeutic bond and may improve adherence; ignoring them will likely lead to therapeutic failure. Numerous studies demonstrate that, even in high-functioning health systems, only ~50% of patients are taking recommended, evidence-based secondary prevention medications, such as statins, by 1 year after a myocardial infarction.

In patients who are eligible for primary prevention strategies, it is important to frame the discussion around the overall evidence base as well as an individual patient’s likelihood of benefit from a given preventive intervention. A first step is to understand the patient’s estimated absolute risk for disease in the foreseeable future, or during their remaining lifespan. However, absolute risk estimation and presentation of those risks is generally insufficient to motivate behavior change. It is critical to assess the patient’s understanding and tolerance of the risk, their readiness to implement lifestyle changes or adhere to drug therapy, and their overall preferences regarding use of drug therapy to prevent an event (e.g., cancer, myocardial infarction, stroke). The clinician can help the patient by informing them of the risks for disease and potential for absolute benefits (and harms) from the available evidence-based choices. This may take more than one conversation, but given that diseases, such as cancer and cardiovascular disease, are the leading causes of premature death and disability, the time is well spent.

Partnering with the patient through motivational interviewing may assist in the process of selecting initial approaches to prevention. Selecting an area that the patient feels they are ready to change can lead to better adherence and greater achievement of success in the short and longer term. If the patient is uncertain what course to choose, prudence would dictate focusing on control of risk factors that may lead to the most rapid reduction in risk for acute events. For example, blood pressure is both a chronic risk factor and an acute trigger for cardiovascular events. Thus, if a patient has both significant elevations in blood pressure and dyslipidemia, it would be appropriate to focus initial efforts on blood pressure control. Likewise, focus on smoking cessation can lead to more rapid reductions in risk for acute events than some other lifestyle interventions.

### ■ PREVENTION AND HEALTH PROMOTION ACROSS THE LIFE COURSE

**Periodic Health Evaluations** The “routine annual physical” has in many ways become an expected part of the patient-physician relationship in primary care practice. However, evidence for the efficacy of the periodic health evaluation in asymptomatic adults unselected for risk factors or disease is mixed, and depends on the outcome. Systematic reviews and meta-analyses of published trials have consistently observed lack of benefit (and also lack of harm) in terms of total mortality in association with periodic health evaluations. Data are more heterogeneous but overall suggest no benefit for cancer- or cardiovascular-specific mortality, with the potential for either benefit or harm depending on number of evaluations and patient-level factors. Well-designed studies on non-fatal clinical events and morbidity have been sparsely reported but there appear to be no large effects.

Periodic health evaluations do appear to lead to greater diagnosis of certain conditions such as hypertension and dyslipidemia, as expected. Likewise, periodic health examinations also improve the delivery of recommended preventive services, such as gynecologic examinations

and Papanicolaou smears, fecal occult blood testing, and cholesterol screening. The benefits and risks associated with screening tests are discussed in detail in **Chap. 4**. Risks of routine evaluations include inappropriate or over-testing, or false-positive findings that require follow-up and induce patients to worry. Periodic health examinations appear to be associated with less patient worry. On balance, given the lack of convincing evidence of harm and the potential for better delivery of appropriate screening, counseling, and preventive services, periodic health evaluations appear reasonable for general populations at average risk for chronic conditions.

It is important to note that routine annual comprehensive physical examinations of asymptomatic adult patients have very low yield and may take an inordinate amount of time in a wellness visit. Such time may be better spent on assessing and counseling the patient on other aspects of their health, as discussed below. Evidence-based components that should be included in periodic evaluations focused on health and prevention include a number of age-appropriate screening tests for chronic disease and risk factors, preventive interventions including immunizations and chemoprevention for at-risk individuals, and preventive counseling. The United States Preventive Services Task Force publishes its *Guide to Clinical Preventive Services*, which contains evidence-based recommendations from the Task Force on preventive services for which there is a high degree of certainty that the service provides at least moderate net clinical benefit (i.e., benefits outweigh harms significantly and to a reasonable magnitude).

**Healthy Behaviors and Lifestyles** Owing to the paucity of evidence, the heterogeneity of study designs and the diverse nature of interventions studied, many clinicians are uncertain as to how to deliver advice regarding healthy behaviors and lifestyles. Nevertheless, adverse behaviors and lifestyles contribute to more than 75% of premature, preventable deaths and disability. Estimates from the US National Health and Nutrition Survey indicate that fewer than 1% of Americans achieve an optimal heart-healthy eating pattern. Thus, whereas there are many demands on time during a typical

patient-clinician encounter, few things may have more impact on longevity, health and quality of life for asymptomatic patients than an efficient approach to assessing, documenting, and improving patients' health behaviors. Indeed, the mere act of assessing health behaviors has been shown to affect patient's health behaviors. Facility with tools for assessment of lifestyle and with strategies for counseling are therefore of paramount importance.

**Healthy Eating Patterns (see Chap. 325)** Despite the existence of numerous "fad" diets, and seemingly inconsistent recommendations on dietary composition, there is remarkable agreement about what should constitute a healthy eating pattern for the broad population to avoid nutritional deficits (i.e., vitamin deficiency) and excesses (i.e., excessive caloric intake) and to maximize potential health (**Table 2-1**). Optimal eating patterns consist of whole fruits and vegetables, whole grains, lean proteins, healthy oils, and allow for non-fat or low-fat dairy intake. They tend to exclude frequent ingestion of foods high in refined sugars and starches, saturated fat, and sodium. Since sodium and refined sugars and starches are the hallmark of much of the processed/packaged food supply, a simple rule of thumb is to provide/cook the majority of one's own meals starting from whole foods and emphasizing fruits and vegetables. Likewise, foods prepared outside of the home tend to have higher fat and sodium content, so special attention to menu choices focused on fruits, vegetables, lean proteins, and whole grains, while minimizing sauces and dressings can help most individuals follow healthier eating patterns. In all cases, sugar-sweetened beverages and non-nutritious snack foods should be minimized. If snacks are included, small amounts of healthy nuts and seeds, or more fruits and vegetables, should be encouraged.

Specific conditions and diseases, such as diabetes, other metabolic disorders, allergies, and gastrointestinal disorders, may require tailored approaches to diet. In counseling most patients, the general approach should focus on whole foods, eating patterns and appropriate calorie balance, rather than on specific micronutrients such as electrolytes or selected vitamins. It should be remembered that most patients have

**TABLE 2-1 Guidelines and Key Recommendations from the Dietary Guidelines for Americans, 2015–2020**

GUIDELINES	KEY RECOMMENDATIONS
<p><b>1. Follow a healthy eating pattern across the lifespan.</b> All food and beverage choices matter. Choose a healthy eating pattern at an appropriate calorie level to help achieve and maintain a healthy body weight, support nutrient adequacy, and reduce the risk of chronic disease.</p> <p><b>2. Focus on variety, nutrient density, and amount.</b> To meet nutrient needs within calorie limits, choose a variety of nutrient-dense foods across and within all food groups in recommended amounts.</p> <p><b>3. Limit calories from added sugars and saturated fats and reduce sodium intake.</b> Consume an eating pattern low in added sugars, saturated fats, and sodium. Cut back on foods and beverages higher in these components to amounts that fit within healthy eating patterns.</p> <p><b>4. Shift to healthier food and beverage choices.</b> Choose nutrient-dense foods and beverages across and within all food groups in place of less healthy choices. Consider cultural and personal preferences to make these shifts easier to accomplish and maintain.</p> <p><b>5. Support healthy eating patterns for all.</b> Everyone has a role in helping to create and support healthy eating patterns in multiple settings nationwide, from home to school to work to communities.</p>	<p>The Dietary Guidelines' Key Recommendations for healthy eating patterns should be applied in their entirety, given the interconnected relationship that each dietary component can have with others.</p> <p><b>Consume a healthy eating pattern that accounts for all foods and beverages within an appropriate calorie level.</b></p> <p><b>A healthy eating pattern includes:</b></p> <ul style="list-style-type: none"> <li>• A variety of vegetables from all of the subgroups—dark green, red and orange, legumes (beans and peas), starchy, and other</li> <li>• Fruits, especially whole fruits</li> <li>• Grains, at least half of which are whole grains</li> <li>• Fat-free or low-fat dairy, including milk, yogurt, cheese, and/or fortified soy beverages</li> <li>• A variety of protein foods, including seafood, lean meats and poultry, eggs, legumes (beans and peas), and nuts, seeds, and soy products</li> <li>• Oils</li> </ul> <p><b>A healthy eating pattern limits:</b></p> <ul style="list-style-type: none"> <li>• Saturated fats and trans fats, added sugars, and sodium</li> </ul> <p>Key Recommendations that are quantitative are provided for several components of the diet that should be limited. These components are of particular public health concern in the United States, and the specified limits can help individuals achieve healthy eating patterns within calorie limits:</p> <ul style="list-style-type: none"> <li>• Consume &lt;10% of calories per day from added sugars</li> <li>• Consume &lt;10% of calories per day from saturated fats</li> <li>• Consume &lt;2300 milligrams (mg) per day of sodium</li> <li>• If alcohol is consumed, it should be consumed in moderation—up to one drink per day for women and up to two drinks per day for men—and only by adults of legal drinking age.</li> </ul> <p>In tandem with the recommendations above, Americans of all ages—children, adolescents, adults, and older adults—should meet the <i>Physical Activity Guidelines for Americans</i> to help promote health and reduce the risk of chronic disease. Americans should aim to achieve and maintain a healthy body weight. The relationship between diet and physical activity contributes to calorie balance and managing body weight. As such, the Dietary Guidelines includes a Key Recommendation to:</p> <p><b>Meet the US Department of Health and Human Services' Physical Activity Guidelines for Americans</b></p>

Source: Adapted from the *Dietary Guidelines for Americans, 2015–2020*. Washington, DC: US Department of Agriculture and US Department of Health and Human Services; 2015. Available at <https://health.gov/dietaryguidelines/2015/guidelines/>.

difficulty understanding nutritional labels on packaged foods, with the attendant demands on numeracy and health literacy.

Dietary guidelines are published by the US Department of Agriculture (USDA) and US Department of Health and Human Services every 5 years, and these guidelines have undergone substantial evolution over time. The current US Dietary Guidelines and Key Recommendations for 2015–2020 are summarized in Table 2-1 and emphasize eating patterns with nutrient-dense (rather than calorie-dense) whole foods, and appropriate caloric intake to achieve and maintain healthy weight. The USDA Guidelines focus on the concept of a healthy plate (rather than the prior food pyramid) for ease of counseling and adoption. Fifty percent of the plate should consist of fruits and vegetables, with remaining portions for whole grains and lean protein foods. When using fat for cooking, it should be done by sauteing in healthier oils (e.g., canola oil), and addition of judicious amounts of healthy raw oils (e.g., olive oil) to dishes is appropriate.

The USDA Guidelines focus on specific healthy eating patterns that adhere to these broad recommendations, and are appropriate for ~97% of the general population. They identify a “Healthy US-Style Eating Pattern” that adheres closely to the evidence-based Dietary Approaches to Stop Hypertension (DASH) eating pattern. Alternative patterns, which vary more in emphasis than in content, include a “Healthy Mediterranean-Style Eating Pattern” and a “Healthy Vegetarian Eating Pattern.”

**AGE- AND SEX-SPECIFIC RECOMMENDATIONS** Current dietary recommendations are generally similar for all life stages from ages ≥2 years, but recommended levels of caloric intake (and hence amounts of foods) differ by age, sex, and physical activity level. For example, recommended caloric intake ranges from 1000 calories/d for sedentary 2-year-old children to as high as 3200 calories/d for active 16- to 18-year-old young men. Recommended caloric intakes peak in the early twenties for men and women and gradually decrease over ensuing decades.

As with all lifestyle counseling aimed at behavior change, dietary approaches that partner with the patient and utilize motivational interviewing strategies and shared goals and commitments tend to work best, as described below (see Approach to the Patient).

**Physical Activity** Similar to the approach to counseling regarding healthy eating patterns, recommendations on participation in physical activity emphasize the point that any physical activity is better than none. A simple rule of thumb for patients is: “If you are doing nothing, do something; and if you are doing something, do more, every day.” The evidence base for physical activity indicates that the marginal benefits from physical activity are greatest in advancing from no activity to low levels of moderate activity. With increasing duration and intensity of activity, there is a continued curvilinear increase in health benefits, but the marginal gains for each additional minute of moderate-to-vigorous activity slowly diminish. Thus, for adults, the optimal amount of physical activity recommended is 150 min of moderate-intensity or 75 min of vigorous intensity aerobic activity per week, performed in episodes of at least 10 min, and preferably spread throughout the week. Additional health benefits can be realized by engaging in physical activity beyond this amount, and/or by adding muscle-strengthening activities that involve all major muscle groups 2 or more days per week.

In counseling patients regarding physical activity, it is important to note that sedentary time (e.g., seated at work, or at home in front of electronic screens) has adverse health consequences independent of the lack of physical activity during these episodes. Therefore, even modest efforts like standing at the desk and doing gentle stretching for periods during the day may be beneficial. It is also important to emphasize that participating in a variety of aerobic activities (biking, swimming, walking, jogging, rowing, elliptical training, stair-climbing, etc.) can be beneficial and may help to avoid overuse injuries and boredom with the exercise regimen. If patients choose to participate in muscle-strengthening activities for health improvement, emphasis should be placed on weights that allow more repetitions (e.g., 3 sets of 15–20 repetitions that can be performed comfortably, with a rest period in between) and on avoiding breath-holding and straining against a closed glottis.

**SUDDEN CARDIAC DEATH RISK** Patients may express concerns regarding the risk of sudden cardiac death during exercise. Whereas the risk of sudden death during exercise does increase directly with the amount of time spent exercising, this association is substantially mitigated by training effects. Thus, patients embarking on an exercise program should be encouraged to increase the duration of aerobic exercise gradually as tolerated, aiming for episodes of at least 30 min 5 times a week as an ideal. Once a comfortable duration is reached, incorporating interval training periods of more intensive activity interspersed during the exercise can provide greater fitness gains.

**EXTREME ENDURANCE ACTIVITIES** As with other forms of exercise, extreme endurance activities such as triathlons and marathons should be undertaken only with appropriate and graded training. Such activities tend to take a greater toll on the musculoskeletal system over time than less extreme activities, and they are also associated with measurable damage to the myocardium and greater risks for other organ damage. Athletes participating in endurance activities routinely have elevations in cardiac troponin (a specific circulating marker of myocardial cell damage and death) at the end of the race, although elevations are lower in those who are well trained. Patients and clinicians should consider the patient’s overall health, specific limitations, potential for injury, and ability to train in decision-making regarding participation in endurance events.

**AGE-SPECIFIC RECOMMENDATIONS** The US Department of Health and Human Services’ *Physical Activity Guidelines for Americans* (Table 2-2) recommend that children and adolescents aged 6–17 years should participate in ≥60 min of physical activity daily, most of which should be moderate- or vigorous-intensity aerobic activity, including vigorous activity at least 3 days a week. As noted above, adults aged 18–64 years are recommended to pursue at least 150 min of moderate-intensity or 75 min of vigorous-intensity aerobic activity per week (or equivalent combinations). Adults aged ≥65 years should follow the adult guidelines, or be as active as possible as abilities and conditions allow. Special emphasis is also placed on exercises to improve balance in those at risk for falling.

**Sleep Hygiene** Sleeping between 7 and 9 h per night appears to be optimal for health in adults aged ≥18 years. Sleeping <7 h is associated with adverse outcomes, including obesity, diabetes, elevated blood pressure, cardiovascular disease, depression, and all-cause mortality, as well as physiologic disturbances such as impaired immune function, increased pain sensitivity, and impaired cognitive performance. Conversely, achieving appropriate levels of sleep is associated with more success in weight loss, better blood pressure control among patients with hypertension, and improved mental health and performance. Regular sleep more than 9 h per night is appropriate for children and adolescents, or individuals recovering from sleep deprivation or illness, but for most individuals the effects on health are uncertain.

Patients often express concerns about the quantity and quality of their sleep. With aging, both aspects of sleep tend to decline, even without overt sleep disorders. Documentation of sleep using a sleep log may assist in understanding different types of insomnia and sleep disorders. Encouraging daily activity to promote fatigue, avoidance of eating and drinking alcohol too close to bedtime, and regular daily sleep habits may help patients achieve better sleep. Regular use of sedative medications should generally be discouraged given the high potential for dependence, addiction, and altered sleep quality.

**DISORDERS OF SLEEP** The prevalence of sleep-related breathing disorders, including obstructive sleep apnea (OSA), is poorly documented. Based on data from the 1990s, the prevalence of diagnosed mild OSA in the US population was ~10%, and of moderate to severe apnea was ~5%. However, the increasing prevalence of obesity, a major risk factor for OSA, suggests that the prevalence may have increased. The prevalence of asymptomatic or undiagnosed sleep apnea is unknown. Patients with persistent complaints of poor sleep quality, excessive daytime somnolence, or with witnessed apneic spells may benefit from screening for sleep disorders, prior to consideration of a formal sleep study. A number of clinical tools have been developed to screen

TABLE 2-2 Recommendations from *Physical Activity Guidelines for Americans*

AGE	RECOMMENDATIONS
6–17 years	<p>Children and adolescents should do 60 min (1 h) or more of physical activity daily.</p> <ul style="list-style-type: none"> <li>• Aerobic: Most of the <math>\geq 60</math> min a day should be either moderate<sup>a</sup> or vigorous-intensity<sup>b</sup> aerobic physical activity, and should include vigorous-intensity physical activity at least 3 days a week.</li> <li>• Muscle-strengthening:<sup>c</sup> As part of their <math>\geq 60</math> min of daily physical activity, children and adolescents should include muscle-strengthening physical activity on at least 3 days of the week.</li> <li>• Bone-strengthening:<sup>d</sup> As part of their <math>\geq 60</math> min of daily physical activity, children and adolescents should include bone-strengthening physical activity on at least 3 days of the week.</li> <li>• It is important to encourage young people to participate in physical activities that are appropriate for their age, that are enjoyable, and that offer variety.</li> </ul>
18–64 years	<ul style="list-style-type: none"> <li>• All adults should avoid inactivity. Some physical activity is better than none, and adults who participate in any amount of physical activity gain some health benefits.</li> <li>• For substantial health benefits, adults should do at least 150 min (2 h and 30 min) a week of moderate-intensity, or 75 min (1 h and 15 min) a week of vigorous-intensity aerobic physical activity, or an equivalent combination of moderate- and vigorous-intensity aerobic activity. Aerobic activity should be performed in episodes of at least 10 min, and preferably, it should be spread throughout the week.</li> <li>• For additional and more extensive health benefits, adults should increase their aerobic physical activity to 300 min (5 h) a week of moderate-intensity, or 150 min a week of vigorous-intensity aerobic physical activity, or an equivalent combination of moderate- and vigorous-intensity activity. Additional health benefits are gained by engaging in physical activity beyond this amount.</li> <li>• Adults should also include muscle-strengthening activities that involve all major muscle groups on <math>\geq 2</math> days a week.</li> </ul>
$\geq 65$ years	<ul style="list-style-type: none"> <li>• Older adults should follow the adult guidelines. When older adults cannot meet the adult guidelines, they should be as physically active as their abilities and conditions will allow.</li> <li>• Older adults should do exercises that maintain or improve balance if they are at risk of falling.</li> <li>• Older adults should determine their level of effort for physical activity relative to their level of fitness.</li> <li>• Older adults with chronic conditions should understand whether and how their conditions affect their ability to do regular physical activity safely.</li> </ul>

<sup>a</sup>Moderate-intensity physical activity: Aerobic activity that increases a person's heart rate and breathing to some extent. On a scale relative to a person's capacity, moderate-intensity activity is usually a 5 or 6 on a 0 to 10 scale. Brisk walking, dancing, swimming, or bicycling on a level terrain are examples. <sup>b</sup>Vigorous-intensity physical activity: Aerobic activity that greatly increases a person's heart rate and breathing. On a scale relative to a person's capacity, vigorous-intensity activity is usually a 7 or 8 on a 0 to 10 scale. Jogging, singles tennis, swimming continuous laps, or bicycling uphill are examples. <sup>c</sup>Muscle-strengthening activity: Physical activity, including exercise that increases skeletal muscle strength, power, endurance, and mass. It includes strength training, resistance training, and muscular strength and endurance exercises. <sup>d</sup>Bone-strengthening activity: Physical activity that produces an impact or tension force on bones, which promotes bone growth and strength. Running, jumping rope, and lifting weights are examples.

Source: Adapted from U.S. Department of Health and Human Services. 2008 *Physical Activity Guidelines for Americans*. Washington, DC: U.S. Department of Health and Human Services; 2008. Available at <http://www.health.gov/paguidelines>.

for sleep apnea, including the Epworth Sleepiness Scale, the STOP (Snoring, Tiredness, Observed apnea, high blood Pressure) Questionnaire, and the STOP-Bang Questionnaire (STOP plus assessment of body mass index, age, neck circumference, and gender), among others. The US Preventive Services Task Force found that current evidence is insufficient to assess the balance of benefits and harms of screening for OSA in asymptomatic adults owing to a lack of validation data in primary care settings. Nonetheless, the high prevalence and significant health consequences of sleep apnea suggest that clinicians should be alert for its potential presence, particularly in patients who are obese with symptoms of excessive daytime somnolence or witnessed apnea episodes. Other sleep disorders, such as restless leg syndrome, may be identified with simple history.

**Weight Management** Overweight and obesity are prevalent in epidemic proportions in the US and other industrialized nations (Chaps. 394, 395). Since 1985, the prevalence of obesity in the United States has increased from ~10% to almost 35%, and the prevalence of overweight is now ~40%. Overweight and obesity disproportionately affect individuals in lower socio-economic strata, and in many underserved minority populations, including African Americans, Latino Americans, and American Indians. In all race-ethnic groups, both overweight and obesity are associated with adverse health consequences, including diabetes, certain cancers, cardiovascular diseases, and degenerative joint disease. Eating disorders such as anorexia and bulimia are much less common but pose major health consequences for affected patients, and should be suspected particularly in younger women with history of rapid weight shifts or underweight status.

Weight loss is one of the most difficult preventive interventions to achieve and sustain over time. However, several key factors can assist the patient and clinician, and early referral to a dietician can be very helpful. The first therapeutic goal is to aim for weight stabilization. Many of the risks of overweight and obesity are driven more strongly by continued weight gain, rather than overweight/obese status per se.

Working with the patient to find initial strategies for weight maintenance can be a successful initial step with success for many patients. For those who can progress to considering weight loss, it is critical to help the patient understand that there is no standard solution. Experimentation and documentation are key. Tools to assist patients can include food and weight logs, activity logs, and smart phone apps. Some patients respond best to structured commercial dietary programs where meals are provided to them. Any of these approaches can be tried with or without social group supports.

The key construct for weight loss is, of course, negative calorie balance. This is achieved through a combination of reduced caloric intake and increased physical activity. Patients may already understand, from prior weight loss attempts, what combination works best for them to achieve this. Some patients find that they cannot lose weight without increasing their exercise. For many, reduction of caloric intake is most efficient. Encouraging the patient to find what works for them is most important. The same principle holds for dietary content. Well done feeding studies indicate that weight loss is dependent far more on the reduction of caloric intake than on the relative composition of fat, protein and carbohydrate in the diet. There may be other medical reasons to choose one approach over another, but if not, encouraging the patient to pick one approach and document the results is an important start.

**Tobacco Cessation (see Chap. 448)** Escaping nicotine dependence is another major, but critical, challenge to prevention and wellness efforts. The addictive effects of nicotine have been well documented, with effects that can last for years after successful cessation. Assessing a patient's past history of cessation attempts and current readiness for change are key first steps in forging a successful approach. Frequent follow-up and reinforcement, as well as use of nicotine replacement therapy and other cessation-promoting medications are additional critical elements. Recidivism is the rule, and patients should expect to resume smoking and attempt again as they journey to tobacco cessation.

## MENTAL HEALTH AND ADDICTION

Assessment for depression and cognitive impairment are important to address when patients exhibit symptoms, or they or their family members express concerns. Both of these common conditions play a major role in reducing quality of life and are high on patients' lists of concerns, even if not clearly expressed. Screening tools for depression are reviewed in [Chap. 444](#). Cognitive function decline with aging or comorbid illness, including depression, should be anticipated. Assessment tools such as the General Practitioner Assessment of Cognition or the Mini-Cog™ test are widely available and effective rapid assessment tools.

**Alcohol and Opioids (see Chaps. 445, 446)** Alcohol dependence and abuse are common and underdiagnosed. Rapid screening tools have proven efficacy for identifying patients with alcohol problems. In a systematic review, the CAGE (cut down, guilty, annoyed, eye opener) questionnaire was most effective at identifying alcohol abuse and dependence, with reasonable sensitivity and high specificity. The present opioid epidemic in the United States presents a new and substantial public health challenge given the high potential for dependency and abuse of these drugs. Rapid screening tools are being developed and validated to assist clinicians in screening for opioid dependence.

## ACCIDENTS AND SUICIDE

Regular assessment of patient safety through simple questions about seat belt use, domestic violence, and gun safety in the home continue to be important parts of health promotion and wellness. Longstanding recommendations for assessment of suicidal ideation among patients with depression or a history of suicide attempts also continue to be relevant.

## APPROACH TO THE PATIENT

In the context of a clinical visit focused on health assessment, health promotion, and prevention, the basic skills of history taking are of paramount importance. Much of the evaluation, counseling, and management that focus on health promotion and prevention also require engagement and buy-in from the patient in order to assist with recognition of contributing behaviors and to promote adherence to therapeutic plans. Therefore, in addition to standard history-taking, additional skills such as motivational interviewing and eliciting patient commitments and contracting may prove of significant value. The availability of additional tools to assist with screening and chronic management, both online and through mobile health technologies, is rapidly expanding, with uncertain implications for the future. Major research gaps exist in our understanding of how best to employ these newer technologies to improve health outcomes. Concepts of behavioral economics are being explored to better understand the psychology of decision-making and incentives as a means to improve lifestyle choices and adherence to treatment plans ([Chap. 468](#)).

The limited time available to clinicians and patients during a wellness visit or periodic health examination (not driven by specific patient issues) makes it important to prioritize assessment and counseling for factors that affect longevity, healthspan, and quality of life over approaches that may have low yield, such as the annual comprehensive physical examination in an asymptomatic patient. Setting clear expectations for the content of a wellness visit may be a first step, and scheduling follow-up visits for findings or to continue indicated counseling are important steps to achieving better health outcomes.

## FURTHER READING

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# 3

## Decision-Making in Clinical Medicine

Daniel B. Mark, John B. Wong

Sir William Osler's familiar quote "Medicine is a science of uncertainty and an art of probability" captures well the complex nature of clinical medicine. Although the science of medicine is often taught as if the mechanisms of the human body operate with Newtonian predictability, every aspect of medical practice is infused with an element of irreducible uncertainty that the clinician ignores at her peril. Clinical medicine has deep roots in science, but it is an imprecise science. More than 100 years after the practice of medicine took its modern form, it remains at its core a craft, to which individual doctors bring varying levels of skill and understanding. With the exponential growth in medical literature and other technical information and an ever increasing number of testing and treatment options, twenty-first century physicians who seek excellence in their craft must master a more diverse and complex set of skills than any of the generations that preceded them. This chapter provides an introduction to three of the pillars upon which the craft of modern medicine rests: (1) expertise in clinical reasoning (what it is and how it can be developed); (2) rational diagnostic tests, use and interpretation; and (3) integration of the best available research evidence with clinical judgment in the care of individual patients (*evidence-based medicine* or EBM and the tools of EBM).

## BRIEF INTRODUCTION TO CLINICAL REASONING

**Clinical Expertise** Defining "clinical expertise" remains surprisingly difficult. Chess has an objective ranking system based on skill and performance criteria. Athletics, similarly, have ranking systems to distinguish novices from Olympians. But in medicine, after physicians complete training and pass the boards (or get recertified), no tests or benchmarks are used to identify those who have attained the highest levels of clinical performance. Physicians often consult a few "elite" clinicians for their "special problem-solving prowess" when particularly difficult or obscure cases have baffled everyone else. Yet despite their skill, even such master clinicians typically cannot explain their exact processes and methods, thereby limiting the acquisition and dissemination of the expertise used to achieve their impressive results. Furthermore, clinical virtuosity appears not to be generalizable, e.g., an expert on hypertrophic cardiomyopathy may be no better (and possibly worse) than a first-year medical resident at diagnosing and managing a patient with neutropenia, fever, and hypotension.

Broadly construed, clinical expertise includes not only cognitive dimensions involving the integration of disease knowledge with verbal and visual cues and test interpretation but also potentially the complex fine-motor skills necessary for invasive procedures and tests. In addition, "the complete package" of expertise in medicine requires effective communication and care coordination with patients and members of the medical team. Research on medical expertise remains sparse overall

and mostly centered on diagnostic reasoning, so in this chapter, we focus primarily on the cognitive elements of clinical reasoning.

Because clinical reasoning occurs in the heads of clinicians, objective study of the process is difficult. One research method used for this area asks clinicians to “think out loud” as they receive increments of clinical information in a manner meant to simulate a clinical encounter. Another research approach focuses on how doctors should reason diagnostically to identify remediable “errors” rather than on how they actually do reason. Much of what is known about clinical reasoning comes from empirical studies of nonmedical problem-solving behavior. Because of the diverse perspectives contributing to this area, with important contributions from cognitive psychology, medical education, behavioral economics, sociology, informatics, and decision sciences, no single integrated model of clinical reasoning exists, and not infrequently, different terms and reasoning models describe similar phenomena.

**Intuitive Versus Analytic Reasoning** A useful contemporary model of reasoning, dual-process theory distinguishes two general systems of cognitive processes. *Intuition* (System 1) provides rapid effortless judgments from memorized associations using pattern recognition and other simplifying “rules of thumb” (i.e., heuristics). For example, a very simple pattern that could be useful in certain situations is “African-American women plus hilar adenopathy equals sarcoid.” Because no effort is involved in recalling the pattern, typically, the clinician is unable to say how those judgments were formulated. In contrast, *Analysis* (System 2), the other form of reasoning in the dual-process model, is slow, methodical, deliberative, and effortful. A student might read about lymph nodes in the lung and from that list (e.g., Chap. 62), identify diseases more common in African-American women or examine the patient for skin or eye findings that may occur with sarcoid. These dual processes, of course, represent two exemplars taken from the cognitive continuum. They provide helpful descriptive insights but very little guidance in how to develop expertise in clinical reasoning. How these idealized systems interact in different decision problems, how experts use them differently from novices, and when their use can lead to errors in judgment remain the subject of study and considerable debate.

Pattern recognition, an important part of System 1 reasoning, is a complex cognitive process that appears largely effortless. One can recognize people’s faces, the breed of a dog, an automobile model, or a piece of music from just a few notes within milliseconds without necessarily being able to articulate the specific features that prompted the recognition. Analogously, experienced clinicians often recognize familiar diagnosis patterns very quickly. The key here is having a large library of stored patterns that can be rapidly accessed. In the absence of an extensive stored repertoire of diagnostic patterns, students (as well as more experienced clinicians operating outside their area of expertise and familiarity) often must use the more laborious System 2 analytic approach along with more intensive and comprehensive data collection to reach the diagnosis.

The following three brief scenarios of a patient with hemoptysis illustrate three distinct patterns that experienced clinicians recognize without effort:

- A 46-year-old man presents to his internist with a chief complaint of hemoptysis. An otherwise healthy, nonsmoker, he is recovering from an apparent viral bronchitis. This presentation pattern suggests that the small amount of blood-streaked sputum is due to acute bronchitis, so that a chest x-ray provides sufficient reassurance that a more serious disorder is absent.
- In the second scenario, a 46-year-old patient who has the same chief complaint but with a 100-pack-year smoking history, a productive morning cough, with blood-streaked sputum, and weight loss fits the pattern of carcinoma of the lung. Consequently, along with the chest x-ray, the clinician obtains a sputum cytology examination and refers this patient for a chest CT scan.
- In the third scenario, the clinician hears a soft diastolic rumbling murmur at the apex on cardiac auscultation in a 46-year-old patient

with hemoptysis who immigrated from a developing country and orders an echocardiogram as well, because of possible pulmonary hypertension from suspected rheumatic mitral stenosis.

Pattern recognition by itself is not, however, sufficient for secure diagnosis. Without deliberative systematic reflection, pattern recognition can result in premature closure: mistakenly jumping to the conclusion that one has correct diagnosis before all the relevant data are in. A critical second step, even when the diagnosis seems obvious, is *diagnostic verification*: considering whether the diagnosis adequately accounts for the presenting symptoms and signs and can explain all the ancillary findings. An example of premature closure is contained in the following case, modified from a real clinical encounter. A 45-year-old man presents with a 3-week history of a “flulike” upper respiratory infection (URI) including dyspnea and a productive cough. The Emergency Department (ED) clinician pulled out a “URI assessment form” which defines and standardizes the information gathered. After quickly acquiring the requisite structured examination components and noting in particular the absence of fever and a clear chest examination, the physician prescribed a cough suppressant for acute bronchitis and reassured the patient that his illness was not serious. Following a sleepless night at home with significant dyspnea, the patient developed nausea and vomiting and collapsed. He was brought back to the ED in cardiac arrest and was unable to be resuscitated. His autopsy showed a posterior wall myocardial infarction (MI) and a fresh thrombus in an atherosclerotic right coronary artery. What went wrong? Presumably, the ED clinician felt that the patient was basically healthy (one can be misled by the way the patient appears on examination—a patient that does not “appear sick” may be incorrectly assumed to have an innocuous illness). So in this case, the physician, upon hearing the overview of the patient from the triage nurse, elected to use the URI assessment protocol even before starting the history, closing consideration of the broader range of possibilities and associated tests required to confirm or refute these possibilities. In particular, by concentrating on the abbreviated and focused URI protocol, the clinician failed to elicit the full dyspnea history, which was precipitated by exertion and accompanied by chest heaviness and relieved by rest, suggesting a far more serious disorder.

Heuristics or rules of thumb are a part of the intuitive system. These cognitive shortcuts provide a quick and easy path to reaching conclusions and making choices, but when used improperly they can lead to errors. Two major research programs have studied heuristics in a mostly non-medical context and have reached very different conclusions about the value of these cognitive tools. The “heuristics and biases” program focuses on how relying on heuristics can lead to cognitive biases and incorrect judgments. Over 100 different cognitive biases have been described. So far, however, there is little evidence that educating physicians and other decision makers to watch for these cognitive biases has any effect on the rate of diagnostic errors. In contrast, the “fast and frugal heuristics” research program explores how and when relying on simple heuristics can produce good decisions. Although many heuristics have relevance to clinical reasoning, only four will be mentioned here.

When diagnosing patients, clinicians usually develop diagnostic hypotheses based on the similarity of that patient’s symptoms, signs and other data to their mental representations (memorized patterns) of the disease possibilities. In other words, clinicians pattern match to identify the diagnoses which share the most similar findings to the patient at hand. This cognitive shortcut is called the representativeness heuristic. Consider a patient with hypertension and headache, palpitations, and diaphoresis. Based on the representativeness heuristic, clinicians might judge pheochromocytoma to be quite likely given this classic presenting symptom triad suggesting pheochromocytoma. Doing so however, would be incorrect given that other causes of hypertension are much more common than pheochromocytoma and this triad of symptoms can occur in patients who do not have it. Thus, clinicians using the representativeness heuristic may overestimate the likelihood of a particular disease based on its representativeness by failing to recognize the low underlying prevalence (i.e., the prior, or

pretest, probabilities). Conversely, atypical presentations of common diseases may lead to underestimating the likelihood of a particular disease. Thus, inexperience with a specific disease and with the breadth of its presentations may also lead to diagnostic delays or errors, e.g., diseases that affect multiple organ systems, such as sarcoid or tuberculosis, may be particularly challenging to diagnose because of the many different patterns they may manifest.

A second commonly used cognitive shortcut, the availability heuristic, involves judgments based on how easily prior similar cases or outcomes can be brought to mind. For example, a clinician may recall a case from a morbidity and mortality conference in which an elderly patient presented with painless dyspnea of acute onset and was evaluated for a pulmonary cause, but eventually found to have acute MI with the diagnostic delay likely contributing to the development of ischemic cardiomyopathy. If the case was associated with a malpractice accusation, such examples may be even more memorable. Errors with the availability heuristic arise from several sources of recall bias. Rare catastrophes are likely to be remembered with a clarity and force disproportionate to their likelihood for future diagnosis—for example, a patient with a sore throat eventually found to have leukemia or a young athlete with leg pain subsequently found to have a sarcoma—and those publicized in the media or recent experience are, of course, easier to recall and therefore more influential on clinical judgments.

The third commonly used cognitive shortcut, the anchoring heuristic (also called conservatism or stickiness), involves insufficiently adjusting the initial probability of disease up (or down) following a positive (or negative test) when compared with Bayes' theorem, i.e., sticking to the initial diagnosis. For example, a clinician may still judge the probability of coronary artery disease (CAD) to be high despite a negative exercise perfusion test and go on to cardiac catheterization (see "Measures of Disease Probability and Bayes' Rule," below).

The fourth heuristic states that clinicians should use the simplest explanation possible that will adequately account for the patient's symptoms and findings (Occam's razor or alternatively the simplicity heuristic). Although this is an attractive and often used principle, it is important to remember that no biologic basis for it exists. Errors from the simplicity heuristic include premature closure leading to the neglect of unexplained significant symptoms or findings.

For complex or unfamiliar diagnostic problems, clinicians typically resort to analytic reasoning processes (System 2) and proceed methodically using the *hypothetico-deductive model of reasoning*. Based on the stated reasons for seeking medical attention, clinicians develop an initial list of diagnostic possibilities in *hypothesis generation*. During the history of the present illness, the initial hypotheses evolve in *diagnostic refinement* as emerging information is tested against the mental models of the diseases being considered with diagnoses increasing and decreasing in likelihood or even being dropped from consideration as the working hypotheses of the moment. These mental models often generate additional questions that distinguish the diagnostic possibilities from one another. The focused physical examination contributes further distinguishing the working hypotheses. Is the spleen enlarged? How big is the liver? Is it tender? Are there any palpable masses or nodules? *Diagnostic verification* involves testing the adequacy (whether the diagnosis accounts for all symptoms and signs) and coherency (whether the signs and symptoms are consistent with the underlying pathophysiological causal mechanism) of the diagnosis. For example, if the enlarged and quite tender liver felt on physical examination is due to acute hepatitis (the hypothesis), then certain specific liver function tests will be markedly elevated (the prediction). Should the tests come back normal, the hypothesis may have to be discarded or substantially modified.

Although often neglected, negative findings are as important as positive ones because they reduce the likelihood of the diagnostic hypotheses under consideration. Chest discomfort that is not provoked or worsened by exertion and not relieved by rest in an active patient reduces the likelihood that chronic ischemic heart disease is the underlying cause. The absence of a resting tachycardia and thyroid gland enlargement reduces the likelihood of hyperthyroidism in a patient with paroxysmal atrial fibrillation.

The acuity of a patient's illness may override considerations of prevalence and the other issues described above. "Diagnostic imperatives" recognize the significance of relatively rare but potentially catastrophic diagnoses if undiagnosed and untreated. For example, clinicians should consider aortic dissection routinely as a possible cause of acute severe chest discomfort. Although the typical presenting symptoms of dissection differ from that of MI, dissection may mimic MI, and because it is far less prevalent and potentially fatal if mistreated, diagnosing dissection remains a challenging diagnostic imperative (Chap. 274). Clinicians taking care of acute, severe chest pain patients should explicitly and routinely inquire about symptoms suggestive of dissection, measure blood pressures in both arms for discrepancies, and examine for pulse deficits. When these are all negative, clinicians may feel sufficiently reassured to discard the aortic dissection hypothesis. If, however, the chest x-ray shows a possible widened mediastinum, the hypothesis should be reinstated and an appropriate imaging test ordered (e.g., thoracic computed tomography [CT] scan or transesophageal echocardiogram). In non-acute situations, the prevalence of potential alternative diagnoses should play a much more prominent role in diagnostic hypothesis generation.

Cognitive scientists studying the thought processes of expert clinicians have observed that clinicians group data into packets, or "chunks," that are stored in short-term or "working memory" and manipulated to generate diagnostic hypotheses. Because short-term memory is limited (classically humans can accurately repeat a list of  $7 \pm 2$  numbers read to them), the number of diagnoses that can be actively considered in hypothesis-generating activities is similarly limited. For this reason, cognitive shortcuts discussed above play a key role in the generation of diagnostic hypotheses, many of which are discarded as rapidly as they are formed, thereby demonstrating that the distinction between analytic and intuitive reasoning is an arbitrary and simplistic, but nonetheless useful, representation of cognition.

Research into the hypothetico-deductive model of reasoning has had difficulty identifying the elements of the reasoning process that distinguish experts from novices. This has led to a shift from examining the problem-solving process of experts to analyzing the organization of their knowledge for pattern matching as exemplars, prototypes, and illness scripts. For example, diagnosis may be based on the resemblance of a new case to patients seen previously (exemplars). As abstract mental models of disease, prototypes incorporate the likelihood of various disease features. Illness scripts include risk factors, pathophysiology, and symptoms and signs. Experts have a much larger store of exemplar and prototype cases, an example of which is the visual long-term memory of experienced radiologists. However, clinicians do not simply rely on literal recall of specific cases but have constructed elaborate conceptual networks of memorized information or models of disease to aid in arriving at their conclusions (illness scripts). That is, expertise involves an enhanced ability to connect symptoms, signs, and risk factors to one another in meaningful ways; relate those findings to possible diagnoses; and identify the additional information necessary to confirm the diagnosis.

No single theory accounts for all the key features of expertise in medical diagnosis. Experts have more knowledge about presenting symptoms of diseases and a larger repertoire of cognitive tools to employ in problem solving than non-experts. One definition of expertise highlights the ability to make powerful distinctions. In this sense, expertise involves a working knowledge of the diagnostic possibilities and those features that distinguish one disease from another. Memorization alone is insufficient, e.g., photographic memory of a medical textbook would not make one an expert. But having access to detailed case-specific relevant information is critically important. In the past, clinicians primarily acquired clinical knowledge through their patient experiences, but now clinicians have access to a plethora of information sources (see Evidence-Based Medicine [EBM] below). Clinicians of the future will be able to leverage the experiences of large numbers of other clinicians using electronic tools, but, as with the memorized textbook, the data alone will be insufficient for becoming an expert. Nonetheless, availability of these data removes one barrier for acquiring experience with connecting symptoms, signs, and risk factors to the possible

diagnoses and identifying the additional distinguishing information necessary to confirm the diagnosis, thereby potentially facilitating the development of the working knowledge necessary for becoming an expert.

Despite all of the research seeking to understand expertise in medicine and other disciplines, it remains uncertain whether any didactic program can actually accelerate the progression from novice to expert or from experienced clinician to master clinician. Deliberate effortful practice (over an extended period of time, sometimes said to be 10 years or 10,000 practice hours) and personal coaching are two strategies that are often used outside medicine (e.g., music, athletics, chess) to promote expertise. Their use in developing medical expertise and maintaining or enhancing it has not yet been adequately explored. Some studies in medicine suggest that didactic education exposing students to both the signs and symptoms of specific diseases and, in addition, the diseases that may present with specific symptoms and signs may be beneficial. Developing a personal learning system (e.g., metacognition) through for example EBM processes below and follow-up to identify diagnoses and treatments for patients that you have cared for provide active learning opportunities.

### ■ DIAGNOSTIC VERSUS THERAPEUTIC DECISION-MAKING

The modern ideal of medical therapeutic decision making is to “personalize” treatment recommendations. In the abstract, personalizing treatment involves combining the best available evidence about what works with an individual patient’s unique features (e.g., risk factors, genomics and co-morbidities) and his or her preferences and health goals to craft an optimal treatment recommendation with the patient. Operationally, two different and complementary levels of personalization are possible: individualizing the risk of harm and benefit for the options being considered based on the specific patient characteristics (precision medicine), and personalizing the therapeutic decision process by incorporating the patient’s preferences and values for the possible health outcomes. This latter process is sometimes referred to as shared decision-making, and typically involves clinicians sharing their knowledge about the options and the associated consequences and tradeoffs, and patients sharing their health goals, e.g., avoiding a short-term risk of dying from coronary artery bypass grafting to see their grandchild get married in a few months.

Individualizing the evidence about therapy **does not** mean relying on physician impressions of benefit and harm from their personal experience. Because of small sample sizes and rare events, the chance of drawing erroneous causal inferences from one’s own clinical experience is very high. For most chronic diseases, therapeutic effectiveness is only demonstrable statistically in large patient populations. It would be incorrect to infer with any certainty, for example, that treating a hypertensive patient with angiotensin-converting enzyme (ACE) inhibitors necessarily prevented a stroke from occurring during treatment, or that an untreated patient would definitely have avoided their stroke had they been treated. For many chronic diseases, a majority of patients will remain event free regardless of treatment choices; some will have events regardless of which treatment is selected; and those who avoided having an event through treatment cannot be individually identified. Blood pressure lowering, a readily observable surrogate endpoint, does not have a tightly coupled relationship with strokes prevented. Consequently, in most situations demonstrating therapeutic effectiveness cannot rely simply on observing the outcome of an individual patient but should instead be based on large groups of patients carefully studied and properly analyzed.

Therapeutic decision-making, therefore, should be based on the best available evidence from clinical trials and well done outcome studies. Trustworthy clinical practice guidelines that synthesize such evidence offer normative guidance for many testing and treatment decisions. However, all guidelines recognize that “one size fits all” recommendations may not apply to individual patients. Increased research into the heterogeneity of treatment effects seeks to understand how best to adjust group level clinical evidence of treatment harms and benefits to account for the absolute level of risks faced by

subgroups and even by individual patients, using, for example, validated clinical risk scores.

### ■ NON-CLINICAL INFLUENCES ON CLINICAL DECISION-MAKING

More than three decades of research on variations in clinician practice patterns has identified important non-clinical forces that shape clinical decisions. These factors can be grouped conceptually into three overlapping categories: (1) factors related to individual physicians practice, (2) factors related to practice setting, and (3) factors related to payment systems.

**Factors Related to Practice Style** To ensure that necessary care is provided at a high level of quality, physicians fulfill a key role in medical care by serving as the patient’s advocate. Factors that influence performance in this role include the physician’s knowledge, training, and experience. Clearly, physicians cannot practice evidence-based medicine if they are unfamiliar with the evidence. As would be expected, specialists generally know the evidence in their field better than do generalists. Beyond published evidence and practice guidelines, a major set of influences on physician practice can be subsumed under the general concept of “practice style.” The practice style serves to define norms of clinical behavior. Beliefs about effectiveness of different therapies and preferred patterns of diagnostic test use are examples of different facets of a practice style. The physician beliefs that drive these different practice styles may be based on training, personal experience, and medical evidence. For example, in heart failure patients, heart failure specialists have more familiarity than general internists with the target doses of ACE inhibitor therapy as defined by large clinical trials and the specific drugs (including adverse effects), and are less likely to overreact to foreseeable problems in therapy such as a rise in creatinine levels or asymptomatic hypotension. Not surprisingly, the specialists are much more likely than generalists to achieve target doses of ACE inhibitor therapy. By contrast, perhaps due to specialization, cardiologists may overestimate the benefit and underestimate the harm of coronary revascularization relative to general internists.

Beyond the patient’s welfare, physician perceptions about the risk of a malpractice suit resulting from either an erroneous decision or a bad outcome may drive clinical decisions and create a practice referred to as defensive medicine. This practice involves using tests and therapies with very small marginal benefits, ostensibly to preclude future criticism should an adverse outcome occur. With conscious or unconscious awareness of a connection to the risk of litigation or to payment, however, over time such patterns of care may become accepted as part of the practice norm, thereby perpetuating their overuse, e.g., annual cardiac exercise testing in asymptomatic patients.

**Practice Setting Factors** Factors in this category relate to work systems including tasks and workflow (interruptions, inefficiencies, workload), technology (poor design or implementation, errors in use, failure, misuse), organizational characteristics (e.g., culture, leadership, staffing, scheduling), and the physical environment (e.g., noise, lighting, layout). Physician-induced demand is a term that refers to the repeated observation that once medical facilities and technologies become available to physicians, they will use them. Other environmental factors that can influence decision-making include the local availability of specialists for consultations and procedures; “high-tech” advanced imaging or procedure facilities such as MRI machines and proton beam therapy centers; and fragmentation of care.

**Payment Systems** Economic incentives are closely related to the other two categories of practice-modifying factors. Financial issues can exert both stimulatory and inhibitory influences on clinical practice. Historically, physicians are paid on a fee-for-service, capitation, or salary basis. In fee-for-service, physicians who do more get paid more, thereby encouraging overuse, consciously or unconsciously. When fees are reduced (discounted reimbursement), clinicians tend to increase the number of services provided to maintain revenue. Capitation, in contrast, provides a fixed payment per patient per year to encourage

physicians to consider a global population budget in managing individual patients and ideally reducing the use of interventions with small marginal benefit. To discourage volume-based excessive utilization, fixed salary compensation plans pay physicians the same regardless of the clinical effort expended, but may provide an incentive to see fewer patients. In recognition of the non-sustainability of continued growth in medical expenditures and the opportunity costs associated with that (funds that might be more beneficially applied to education, energy, social welfare or defense), current efforts seek to transition to a value-based payment system to reduce overuse and to reflect benefit. Work to define how to actually tie payment to value has mostly focused so far on “pay for performance” models. High quality clinical trial evidence for the effectiveness of these models is still mostly lacking.

### ■ INTERPRETATION OF DIAGNOSTIC TESTS

Despite impressive technological advances in medicine over the last century, uncertainty still abounds and challenges all aspects of medical decision-making. Compounding this challenge, massive information overload characterizes modern medicine. Clinicians on average subscribe to seven journals, presenting them with over 2500 new articles each year, and need access to 2 million pieces of information to practice medicine. Of course, to be useful, this information must be sifted for quality and examined for applicability for integration into patient-specific care. Although computers appear to offer an obvious solution both for information management and for quantification of medical care uncertainties, many practical problems must be solved before computerized decision support can be routinely incorporated into the clinical reasoning process in a way that demonstrably improves the quality of care. For the present, understanding the nature of diagnostic test information can help clinicians become more efficient users of such data. The next section reviews concepts related to diagnostic testing.

### ■ DIAGNOSTIC TESTING: MEASURES OF TEST ACCURACY

The purpose of performing a test on a patient is to reduce uncertainty about the patient’s diagnosis or prognosis in order to facilitate appropriate management. Although diagnostic tests commonly refer to laboratory (e.g., blood count) or imaging tests or procedures (e.g., colonoscopy or bronchoscopy), any information that changes a provider’s understanding of the patient’s problem qualifies as a diagnostic test. Thus, even the history and physical examination should be considered as diagnostic tests. In clinical medicine, it is common to reduce the results of a test to a dichotomous outcome, such as positive or negative, normal or abnormal. Although this simplification ignores useful information (such as the degree of abnormality), it facilitates illustrating some important principles of test interpretation which are described below.

The accuracy of any diagnostic test is assessed relative to a “gold standard,” where a positive gold standard test defines the patients who have disease and a negative test rules out disease (Table 3-1). Characterizing the diagnostic performance of a new test requires identifying an appropriate population (ideally, patients representative of those in whom the new test would be used) and applying both the new and the gold standard tests to all subjects. Biased estimates of test performance

TABLE 3-1 Measures of Diagnostic Test Accuracy		
TEST RESULT	DISEASE STATUS	
	PRESENT	ABSENT
Positive	True positives (TP)	False positives (FP)
Negative	False negatives (FN)	True Negatives (TN)
<b>Test Characteristics in Patients with Disease</b>		
True-positive rate (sensitivity) = $TP / (TP + FN)$		
False-negative rate = $FN / (TP + FN) = 1 - \text{true positive rate}$		
<b>Test Characteristics in Patients without Disease</b>		
True-negative rate (specificity) = $TN / (TN + FP)$		
False-positive rate = $FP / (TN + FP) = 1 - \text{true-negative rate}$		

occur when diagnostic accuracy is defined using an inappropriate population or one in which gold standard determination of disease status is incomplete. The accuracy of the new test in distinguishing disease from health is determined relative to the gold standard results and summarized in four estimates. The sensitivity or true-positive rate of the new test reflects how well the new test identifies patients with disease. It is the proportion of patients with disease (defined by the gold standard) who have a positive test. The proportion of patients with disease who have a negative test is the false-negative rate, calculated as  $1 - \text{sensitivity}$ . The specificity, or true-negative rate reflects how well the new test correctly identifies patients without disease. It is the proportion of patients without disease (defined by the gold standard) who have a negative test. The proportion of patients without disease who have positive test is the false-positive rate, calculated as  $1 - \text{specificity}$ . In theory, a perfect test would be one with a sensitivity of 100% and a specificity of 100% and would completely distinguish patients with disease from those without it. A useful mnemonic is the following: a *negative* high sensitivity (*Sn*) test helps rule out disease (Negative *Sn*Out), and a *positive* high specificity (*Sp*) test helps rule in disease (Positive *Sp*In).

Calculating sensitivity and specificity requires selection of a threshold value or cut point above which the test is considered “positive.” Making the cut point “stricter” (e.g., raising it) lowers sensitivity but improves specificity, while making it “laxer” (e.g., lowering it) raises sensitivity but lowers specificity. This dynamic trade-off between more accurate identification of subjects with disease versus those without disease is often displayed graphically as a receiver operating characteristic (ROC) curve (Fig. 3-1) by plotting sensitivity (*y* axis) versus  $1 - \text{specificity}$  (*x* axis). Each point on the curve represents a potential cut point with an associated sensitivity and specificity value. The area under the ROC curve often is used as a quantitative measure of the information content of a test. Values range from 0.5 (no diagnostic information from testing at all; the test is equivalent to flipping a coin) to 1.0 (perfect test). The choice of cut point should in theory reflect the relative harms and benefits of treatment for those without versus those with disease. For example, if treatment was safe with substantial benefit, then choosing a high sensitivity cut point (upper right of the ROC curve) for a low risk test may be appropriate (e.g., phenylketonuria in newborns), but if treatment had substantial risk for harm, then

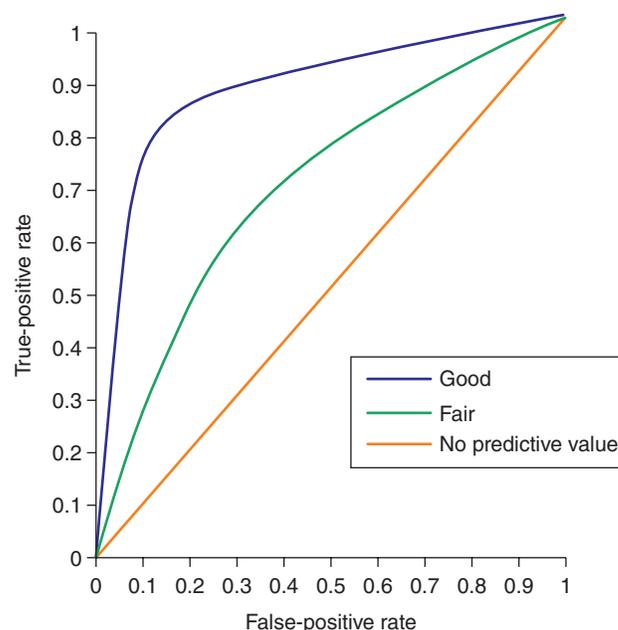


FIGURE 3-1 Each receiver operating characteristic (ROC curve) illustrates a trade-off that occurs between improved test sensitivity (accurate detection of patients with disease) and improved test specificity (accurate detection of patients without disease), as the test value defining when the test turns from “negative” to “positive” is varied. A 45° line would indicate a test with no predictive value (sensitivity = specificity at every test value). The area under each ROC curve is a measure of the information content of the test. Thus, a larger ROC area signifies increased diagnostic accuracy.

choosing a high specificity cut point (lower left of the ROC curve) may be appropriate (e.g., chemotherapy for cancer). The choice of cut point may also depend on the likelihood of disease with low likelihoods placing a greater emphasis on the harms of false positive tests (e.g., HIV testing in marriage applicants) or the harms of false-negative tests (e.g., HIV testing in blood donors).

### ■ MEASURES OF DISEASE PROBABILITY AND BAYES' RULE

In the absence of perfect tests, the true disease state of the patient remains uncertain after every test. Bayes' rule provides a way to quantify the revised uncertainty using simple probability mathematics (and thereby avoid anchoring bias). It calculates the *posttest probability* or likelihood of disease after a test result, from three parameters: the pretest probability of disease, the test sensitivity, and the test specificity. The *pretest probability* is a quantitative estimate of the likelihood of the diagnosis before the test is performed and is usually estimated from the prevalence of the disease in the underlying population (if known) or clinical context (e.g., age, sex and type of chest pain). For some common conditions, such as CAD, existing nomograms and statistical models generate estimates of pretest probability that account for history, physical examination, and test findings. The posttest probability (also called the predictive value of the test, see below) is a recalibrated statement of the likelihood of the diagnosis, accounting for both pretest probability and test results. For the likelihood of disease following a positive test (i.e., positive predictive value), Bayes' rule is calculated as:

$$\text{Posttest probability} = \frac{\text{Pretest probability} \times \text{test sensitivity}}{\text{Pretest probability} \times \text{test sensitivity} + (1 - \text{Pretest probability}) \times \text{test false-positive rate}}$$

For example, consider a 64-year-old woman with atypical chest pain who has a pretest probability of 0.50 and a "positive" diagnostic test result (assuming test sensitivity = 0.90 and specificity = 0.90).

$$\text{Posttest probability} = \frac{(0.50)(0.90)}{(0.50)(0.90) + (0.50)(0.10)} = 0.90$$

The term predictive value has often been used as a synonym for the posttest probability. Unfortunately, clinicians commonly misinterpret reported predictive values as intrinsic measures of test accuracy rather than calculated probabilities. Studies of diagnostic test performance compound the confusion by calculating predictive values from the same sample used to measure sensitivity and specificity. Such calculations are misleading unless the test is applied subsequently to populations with exactly the same disease prevalence. For these reasons, the term predictive value is best avoided in favor of the more descriptive posttest probability following a positive or a negative test result.

The nomogram version of Bayes' rule (Fig. 3-2) helps us to understand at a conceptual level how it estimates the posttest probability of disease. In this nomogram, the impact of the diagnostic test result is summarized by the likelihood ratio, which is defined as the ratio of the probability of a given test result (e.g., "positive" or "negative") in a patient with disease to the probability of that result in a patient without disease, thereby providing a measure of how well the test distinguishes those with from those without disease.

The *likelihood ratio for a positive test* is calculated as the ratio of the true-positive rate to the false-positive rate (or sensitivity/[1 – specificity]). For example, a test with a sensitivity of 0.90 and a specificity of 0.90 has a likelihood ratio of 0.90/(1 – 0.90), or 9. Thus, for this hypothetical test, a "positive" result is 9 times more likely in a patient with the disease than in a patient without it. Most tests in medicine have likelihood ratios for a positive result between 1.5 and 20. Higher values are associated with tests that more substantially increase the posttest likelihood of disease. A very high likelihood ratio positive (>10) usually implies

high specificity, so a positive high specificity test helps "rule in" disease. If sensitivity is excellent but specificity is less so, the likelihood ratio will be reduced substantially (e.g., with a 90% sensitivity but a 55% specificity, the likelihood ratio positive is 2.0).

The corresponding *likelihood ratio for a negative test* is the ratio of the false-negative rate to the true-negative rate (or [1 – sensitivity]/specificity). Lower likelihood ratio negative values more substantially lower the posttest likelihood of disease. A very low likelihood ratio negative (falling below 0.10) usually implies high sensitivity, so a negative high sensitivity test helps "rule out" disease. The hypothetical test considered above with a sensitivity of 0.9 and a specificity of 0.9 would have a likelihood ratio for a negative test result of (1 – 0.9)/0.9, or 0.11, meaning that a negative result is about one-tenth as likely in patients with disease than in those without disease (or about ten times more likely in those without disease than in those with disease).

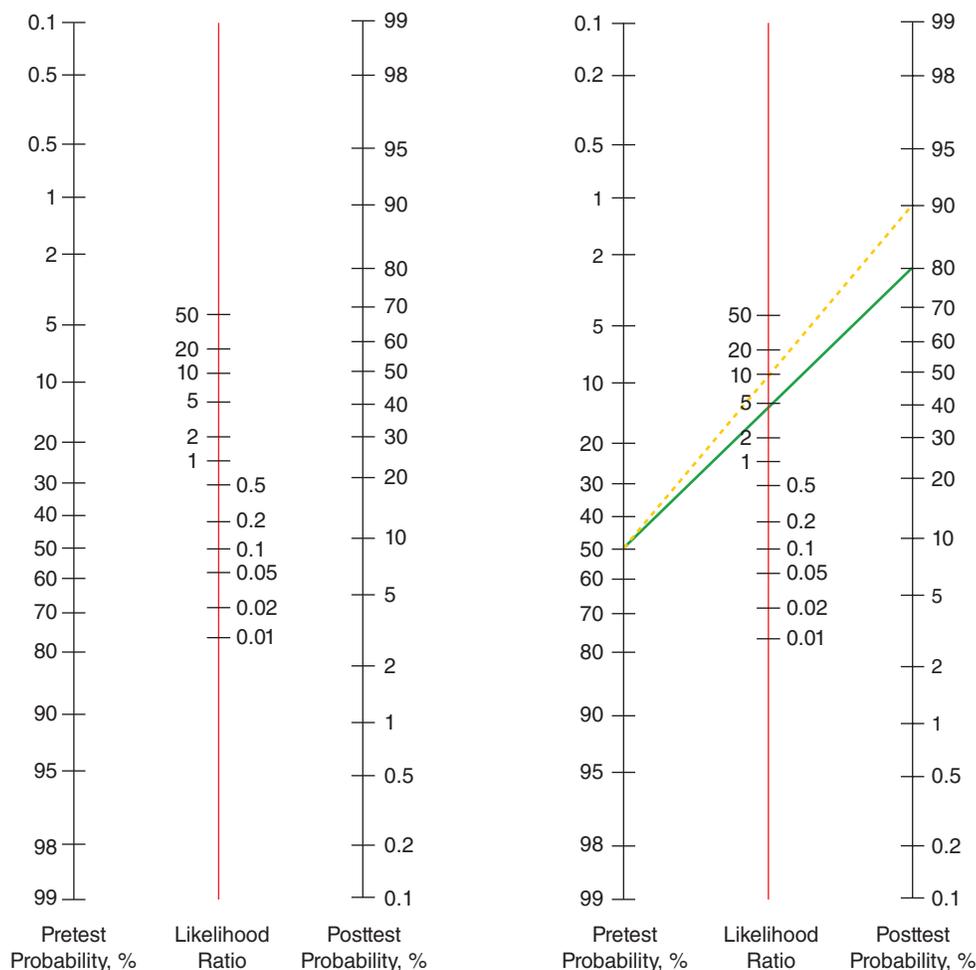
### ■ APPLICATIONS TO DIAGNOSTIC TESTING IN CAD

Consider two tests commonly used in the diagnosis of CAD: an exercise treadmill and an exercise single-photon emission CT (SPECT) myocardial perfusion imaging test (Chap. 236). Meta-analysis has shown that a positive treadmill ST-segment response has an average sensitivity of 60% and an average specificity of 75%, yielding a likelihood ratio positive of 2.4 (0.60/[1 – 0.75]) (consistent with modest discriminatory ability because it falls between 2 and 5). For a 41-year-old man with nonanginal pain and a 10% pretest probability of CAD, the posttest probability of disease after a positive result rises to only about 30%. For a 60-year-old woman with typical angina and a pretest probability of CAD of 80%, a positive test result raises the posttest probability of disease to about 95%.

In contrast, exercise SPECT myocardial perfusion test is more accurate for diagnosis of CAD. For simplicity, assume that the finding of a reversible exercise-induced perfusion defect has both a sensitivity and a specificity of 90% (a bit higher than reported), yielding a likelihood ratio for a positive test of 9.0 (0.90/[1 – 0.90]) (consistent with intermediate discriminatory ability because it falls between 5 and 10). For the same 10% pretest probability patient, a positive test raises the probability of CAD to 50% (Fig. 3-2). However, despite the differences in posttest probabilities between these two tests (30 versus 50%), the more accurate test may not improve diagnostic likelihood enough to change patient management (e.g., decision to refer to cardiac catheterization) because the more accurate test has only moved the physician from being fairly certain that the patient did not have CAD to a 50:50 chance of disease. In a patient with a pretest probability of 80%, exercise SPECT test raises the posttest probability to 97% (compared with 95% for the exercise treadmill). Again, the more accurate test does not provide enough improvement in posttest confidence to alter management, and neither test has improved much on what was known from clinical data alone.

In general, positive results with an accurate test (e.g., likelihood ratio positive 10) when the pretest probability is low (e.g., 20%) do not move the posttest probability to a range high enough to rule in disease (e.g., 80%). In screening situations, pretest probabilities are often particularly low because patients are asymptomatic. In such cases, specificity becomes particularly important. For example, in screening first-time female blood donors without risk factors for HIV, a positive test raised the likelihood of HIV to only 67% despite a specificity of 99.995% because the prevalence was 0.01%. Conversely, with a high pretest probability, a negative test may not rule out disease adequately if it is not sufficiently sensitive. Thus, the largest change in diagnostic likelihood following a test result occurs when the clinician is most uncertain (i.e., pretest probability between 30 and 70%). For example, if a patient has a pretest probability for CAD of 50%, a positive exercise treadmill test will move the posttest probability to 80% and a positive exercise SPECT perfusion test will move it to 90% (Fig. 3-2).

As presented above, Bayes' rule employs a number of important simplifications that should be considered. First, few tests provide only "positive" or "negative" results. Many tests have multi-dimensional outcomes (e.g., extent of ST-segment depression, exercise duration, and exercise-induced symptoms with exercise testing). Although Bayes'



**FIGURE 3-2** Nomogram version of Bayes' theorem used to predict the posttest probability of disease (right-hand scale) using the pretest probability of disease (left-hand scale) and the likelihood ratio for a positive test (middle scale). See text for information on calculation of likelihood ratios. To use, place a straightedge connecting the pretest probability and the likelihood ratio and read off the posttest probability. The right-hand part of the figure illustrates the value of a positive exercise treadmill test (likelihood ratio 4, green line) and a positive exercise thallium single-photon emission CT perfusion study (likelihood ratio 9, broken yellow line) in a patient with a pretest probability of coronary artery disease of 50%. (Adapted from Centre for Evidence-Based Medicine: Likelihood ratios. Available at <http://www.cebm.net/likelihood-ratios/>.)

theorem can be adapted to this more detailed test result format, it is computationally more complex to do so. Similarly, when multiple sequential tests are performed, the posttest probability may be used as the pretest probability to interpret the second test. However, this simplification assumes conditional independence—that is, that the results of the first test do not affect the likelihood of the second test result—and this is often not true.

Finally, many texts assert that sensitivity and specificity are prevalence-independent parameters of test accuracy. This statistically useful assumption, however, is clinically simplistic. A treadmill exercise test, for example, has a sensitivity of ~30% in a population of patients with 1-vessel CAD, whereas its sensitivity in patients with severe 3-vessel CAD approaches 80%. Thus, the best estimate of sensitivity to use in a particular decision may vary, depending on the severity of disease in the local population. A hospitalized, symptomatic, or referral population typically has a higher prevalence of disease and, in particular, a higher prevalence of more advanced disease than does an outpatient population. Consequently, test sensitivity will likely be higher in hospitalized patients, and test specificity higher in outpatients.

### ■ STATISTICAL PREDICTION MODELS

Bayes' rule, when used as presented above, is useful in studying diagnostic testing concepts but may prove too simplistic for use in actual patient care decisions. Predictions based on multivariable statistical models can more accurately address these more complex problems

by simultaneously accounting for additional relevant patient characteristics. In particular, these models explicitly account for multiple, even possibly overlapping, pieces of patient-specific information and assign a relative weight to each on the basis of its unique independent contribution to the prediction in question. For example, a logistic regression model to predict the probability of CAD ideally considers all the relevant independent factors from the clinical examination and diagnostic testing and their relative importance instead of the limited data that clinicians can manage in their heads or with Bayes' rule. However, despite this strength, prediction models are usually too complex computationally to use without a calculator or computer. Guideline-driven treatment recommendations based on statistical prediction models available online, e.g., the ACC/AHA risk calculator for primary prevention with statins and the CHA<sub>2</sub>DS<sub>2</sub>-VASC calculator for anticoagulation for atrial fibrillation have generated more widespread usage. Whether the adoption of electronic health records will promote more use of predictive models in clinical practice and increase their impact on clinical encounters and outcomes remains unclear.

One reason for limited clinical use is that, to date, only a handful of prediction models have been validated properly (for example, Wells' criteria for pulmonary embolism, see Table 3-2). The importance of independent validation in a population separate from the one used to develop the model cannot be overstated. An unvalidated prediction model should be viewed with the skepticism appropriate for any new

drug or medical device that has not had rigorous clinical trial testing.

When statistical survival models in cancer and heart disease have been compared directly with clinicians' predictions, the survival models have been found to be more consistent, as would be expected but not always more accurate. On the other hand, comparison of clinicians with websites and apps that generate lists of possible diagnoses to help patients with self-diagnosis found that physicians outperformed the currently available programs. For students and less-experienced

**TABLE 3-2** Wells Clinical Prediction Rule for Pulmonary Embolism

CLINICAL FEATURE	POINTS
Clinical signs of deep-vein thrombosis	3
Alternative diagnosis is less likely than PE	3
Heart rate >100 beats per min	1.5
Immobilization ≥3 d or surgery in previous 4 weeks	1.5
History of deep-vein thrombosis or pulmonary embolism	1.5
Hemoptysis	1
Malignancy (with treatment within 6 months) or palliative	1
INTERPRETATION	
Score >6.0	High
Score 2.0–6.0	Intermediate
Score <2.0	Low

clinicians, the biggest value of diagnostic decision support may be in extending diagnostic possibilities and triggering “rational override” but their impact on knowledge, information-seeking, and problem-solving needs additional research.

## FORMAL DECISION SUPPORT TOOLS

### ■ DECISION SUPPORT SYSTEMS

Over the last 40 years, many attempts have been made to develop computer systems to aid clinical decision-making and patient management. Conceptually, computers offer several levels of potentially useful support for clinicians. At the most basic level, they provide ready access to vast reservoirs of information, which may, however, be quite difficult to sort through to find what is needed. At higher levels, computers can support care management decisions by making accurate predictions of outcome, or can simulate the whole decision process, and provide algorithmic guidance. Computer-based predictions using Bayesian or statistical regression models inform a clinical decision but do not actually reach a “conclusion” or “recommendation.” Machine learning methods are being applied to pattern recognition tasks such as the examination of skin lesions and the interpretation of x-rays. Artificial intelligence systems attempt to simulate or replace human reasoning with a computer-based analogue. To date, such approaches have achieved only limited success. Reminder or protocol-directed systems do not make predictions but use existing algorithms, such as guidelines or appropriate utilization criteria, to direct clinical practice. In general, however, decision support systems have had little impact on practice. Reminder systems built into electronic health records have shown the most promise, particularly in correcting drug dosing and promoting adherence to guidelines. Checklists may also help avoid or reduce errors.

### ■ DECISION ANALYSIS

Compared with the decision support methods above, decision analysis represents a normative prescriptive approach to decision-making in the face of uncertainty. Its principal application is in complex decisions. For example, public health policy decisions often involve *trade-offs* in length versus quality of life, benefits versus resource use, population versus individual health, and *uncertainty* regarding efficacy, effectiveness, and adverse events as well as *values* or preferences regarding mortality and morbidity outcomes.

One recent analysis using this approach involved the optimal screening strategy for breast cancer, which has remained controversial, in part because a randomized controlled trial to determine when to begin screening and how often to repeat screening mammography is impractical. In 2016, the National Cancer Institute sponsored Cancer Intervention and Surveillance Network (CISNET) examined eight strategies differing by whether to initiate mammography screening at age 40, 45, or 50 years and whether to screen annually, biennially, or annually for women in their forties and biennially thereafter (hybrid). The six simulation models found biennial strategies to be the most efficient for average-risk women. Biennial screening for 1000 women from age 50 to 74 years versus no screening avoided seven breast cancer deaths. Screening annually from age 40 to 74 years avoided three additional deaths but required 20,000 additional mammograms and yielded 1988 more false-positive results. Factors that influenced the results included patients with a 2–4-fold higher risk for developing breast cancer in whom annual screening from 40 to 74 yielded similar benefits as biennial screening from age 50 to 74. For average-risk patients with moderate or severe co-morbidities, screening could be stopped earlier at ages 66–68 years.

This analysis involved six models that reproduced epidemiologic trends and a screening trial result, accounted for digital technology and treatments advances, and considered quality of life, risk factors, breast density, and comorbidity. It provided novel insights into a public health problem in the absence of a randomized clinical trial and helped weigh the pros and cons of such a health policy recommendation. Although such models have been developed for selected clinical problems, their benefit and application to individual real-time clinical management has yet to be demonstrated.

## DIAGNOSIS AS AN ELEMENT OF QUALITY OF CARE

High quality medical care begins with accurate diagnosis. The incidence of diagnostic errors has been estimated by a variety of methods including postmortem examinations, medical record reviews, and medical malpractice claims, with each yielding complementary but different estimates of this quality of care patient-safety problem. In the past, diagnostic errors tended to be viewed as a failure of individual clinicians. The modern view is that they are mostly system of care deficiencies. Current estimates suggest that nearly everyone will experience at least one diagnostic error in their lifetime, leading to mortality, morbidity, unnecessary tests and procedures, costs, and anxiety.

Solutions to the “diagnostic errors as a system of care problem” have focused on system-level approaches, such as decision support and other tools integrated into electronic medical records. The use of checklists has been proposed as a means of reducing some of the cognitive errors discussed earlier in the chapter, such as premature closure. While checklists have been shown useful in certain medical contexts, such as the ORs and ICUs, their value in preventing diagnostic errors that lead to patient adverse events remains to be shown.

## EVIDENCE-BASED MEDICINE

Clinical medicine is defined traditionally as a practice combining medical knowledge (including scientific evidence), intuition, and judgment in the care of patients (Chap. 1). Evidence-based medicine (EBM) updates this construct by placing much greater emphasis on the processes by which clinicians gain knowledge of the most up-to-date and relevant clinical research to determine for themselves whether medical interventions alter the disease course and improve the length or quality of life. The meaning of practicing EBM becomes clearer through an examination of its four key steps:

1. Formulating the management question to be answered
2. Searching the literature and online databases for applicable research data
3. Appraising the evidence gathered with regard to its validity and relevance
4. Integrating this appraisal with knowledge about the unique aspects of the patient (including the patient’s preferences about the possible outcomes)

The process of searching the world’s research literature and appraising the quality and relevance of studies can be time-consuming and requires skills and training that most clinicians do not possess. Thus, identifying recent systematic overviews of the problem in question (Table 3-3) may offer the best starting point for most EBM searches. However, the medical literature is now being flooded with systematic reviews of varying quality and clinical utility. Therefore, systematic reviews should be used in conjunction with selective reading of some of the best empirical studies.

Generally, the EBM tools listed in Table 3-3 provide access to research information in one of two forms. The first, primary research reports, is the original peer-reviewed research work that is published in medical journals and accessible through MEDLINE in abstract form. However, without training in using MEDLINE, locating reports quickly and efficiently that are on point in a sea of irrelevant or unhelpful citations remains difficult, and important studies are easily missed. Systematic reviews, the second form, are regarded by some as the highest level of evidence in the hierarchy because they are intended to comprehensively summarize the available evidence on a particular topic. To avoid the potential biases found in review articles, predefined reproducible explicit search strategies and inclusion and exclusion criteria seek to find all of the relevant scientific research and grade its quality. The prototype for this kind of resource is the Cochrane Database of Systematic Reviews. When appropriate, a meta-analysis is used to quantitatively summarize the systematic review findings. The next two sections explicate the major types of clinical research reports available in the literature and the process of aggregating those data into meta-analyses.

TABLE 3-3 Selected Tools for Finding the Evidence in Evidence-Based Medicine

NAME	DESCRIPTION	WEB ADDRESS	AVAILABILITY
Evidence-Based Medicine Reviews	Comprehensive electronic database that combines and integrates: 1. The Cochrane Database of Systematic Reviews 2. ACP Journal Club 3. The Database of Abstracts of Reviews of Effectiveness	<a href="http://www.ovid.com">www.ovid.com</a>	Subscription required. Available through medical center libraries and other institutions.
Cochrane Library	Collection of EBM databases, including the Cochrane Database of Systematic Reviews—full text articles reviewing specific health care topics	<a href="http://www.cochrane.org">www.cochrane.org</a>	Subscription required. Abstracts of systematic reviews available free online. Some countries have funding to provide free access to all residents.
ACP Journal Club	Collection of summaries of original studies and systematic reviews. Published bimonthly. All data since 1991 available on website, updated yearly.	<a href="http://www.acpjc.org">www.acpjc.org</a>	Subscription required.
Clinical Evidence	Monthly updated directory of concise overviews of common clinical interventions.	<a href="http://www.clinicalevidence.com">www.clinicalevidence.com</a>	Subscription required. Free access for United Kingdom and developing countries.
MEDLINE	National Library of Medicine database with citations back to 1966.	<a href="http://www.nlm.nih.gov">www.nlm.nih.gov</a>	Free via Internet.

### ■ SOURCES OF EVIDENCE: CLINICAL TRIALS AND REGISTRIES

The notion of learning from observation of patients is as old as medicine itself. Over the last 50 years, physicians' understanding of how best to turn raw observation into useful evidence has evolved considerably. Case reports, personal anecdotal experience, and small single-center case series are now recognized as having severe limitations in validity and generalizability, and although they may generate hypotheses or be the first reports of adverse events or therapeutic benefit, they have no role in formulating modern standards of practice. The major tools used to develop reliable evidence consist of the randomized clinical trial and the large observational registry. A registry or database typically is focused on a disease or syndrome (e.g., different types of cancer, acute or chronic CAD, pacemaker capture or chronic heart failure), a clinical procedure (e.g., bone marrow transplantation, coronary revascularization), or an administrative process (e.g., claims data used for billing and reimbursement).

By definition, in observational data, the investigator does not control patient care. Carefully collected prospective observational data, however, can at times achieve a level of evidence quality approaching that of major clinical trial data. At the other end of the spectrum, data collected retrospectively (e.g., chart review) are limited in form and content to what previous observers recorded and may not include the specific research data being sought (e.g., claims data). Advantages of observational data include the inclusion of a broader population as encountered in practice than is typically represented in clinical trials because of their restrictive inclusion and exclusion criteria. In addition, observational data provide primary evidence for research questions when a randomized trial cannot be performed. For example, it would be difficult to randomize patients to test diagnostic or therapeutic strategies that are unproven but widely accepted in practice, and it would be unethical to randomize based on sex, racial/ethnic group, socioeconomic status, or country of residence or to randomize patients to a potentially harmful intervention, such as smoking or deliberately overeating to develop obesity.

A well-done prospective observational study of a particular management strategy differs from a well-done randomized clinical trial most importantly by its lack of protection from treatment selection bias. The use of observational data to compare diagnostic or therapeutic strategies assumes that sufficient uncertainty and heterogeneity exists in clinical practice to ensure that similar patients will be managed differently by diverse physicians. In short, the analysis assumes that a sufficient element of randomness (in the sense of disorder rather than in the formal statistical sense) exists in clinical management. In such cases, statistical models attempt to adjust for important imbalances to "level the playing field" so that a fair comparison among treatment options can be made. When management is clearly not random (e.g., all eligible left main CAD patients are referred for coronary bypass

surgery), the problem may be too confounded (biased) for statistical correction, and observational data may not provide reliable evidence.

In general, the use of concurrent controls is vastly preferable to that of historical controls. For example, comparison of current surgical management of left main CAD with medically treated patients with left main CAD during the 1970s (the last time these patients were routinely treated with medicine alone) would be extremely misleading because "medical therapy" has substantially improved in the interim.

Randomized controlled clinical trials include the careful prospective design features of the best observational data studies but also include the use of random allocation of treatment. This design provides the best protection against measured and unmeasured confounding due to treatment selection bias (a major aspect of internal validity). However, the randomized trial may not have good external validity (generalizability) if the process of recruitment into the trial resulted in the exclusion of many potentially eligible subjects or if the nominal eligibility for the trial describe a very heterogeneous population.

Consumers of medical evidence need to be aware that randomized trials vary widely in their quality and applicability to practice. The process of designing such a trial often involves many compromises. For example, trials designed to gain U.S. Food and Drug Administration (FDA) approval for an investigational drug or device must fulfill regulatory requirements (such as the use of a placebo control) that may result in a trial population and design that differs substantially from what practicing clinicians would find most useful.

### ■ META-ANALYSIS

The Greek prefix *meta* signifies something at a later or higher stage of development. Meta-analysis is research that combines and summarizes the available evidence quantitatively. Although it is used to examine nonrandomized studies, meta-analysis is most useful for summarizing all randomized trials examining a particular therapy. Ideally, unpublished trials should be identified and included to avoid publication bias (i.e., missing "negative" trials which may not be published). Furthermore, the best meta-analyses obtain and analyze individual patient-level data from all trials rather than using only the summary data from published reports. Nonetheless, not all published meta-analyses yield reliable evidence for a particular problem, so their methodology should be scrutinized carefully to ensure proper study design and analysis. The results of a well-done meta-analysis are likely to be most persuasive if they include at least several large-scale, properly performed randomized trials. Meta-analysis can especially help detect benefits when individual trials are inadequately powered (e.g., the benefits of streptokinase thrombolytic therapy in acute MI demonstrated by ISIS-2 in 1988 were evident by the early 1970s through meta-analysis). However, in cases in which the available trials are small or poorly done, meta-analysis should not be viewed as a remedy for deficiencies in primary trial data or trial design.

Meta-analyses typically focus on summary measures of relative treatment benefit, such as odds ratios or relative risks. Clinicians also should examine what absolute risk reduction (ARR) can be expected from the therapy. A summary metric of absolute treatment benefit is the number needed to treat (NNT) to prevent one adverse outcome event (e.g., death, stroke). NNT is simply  $1/ARR$ . For example, if a hypothetical therapy reduced mortality rates over a 5-year follow-up by 33% (the relative treatment benefit) from 12% (control arm) to 8% (treatment arm), the absolute risk reduction would be  $12\% - 8\% = 4\%$  and the NNT would be  $1/.04$ , or 25. Thus, it would be necessary to treat 25 patients for 5 years to prevent 1 death. If the hypothetical treatment was applied to a lower-risk population, say, with a 6% 5-year mortality, the 33% relative treatment benefit would reduce absolute mortality by 2% (from 6 to 4%), and the NNT for the same therapy in this lower-risk group of patients would be 50. Although not always made explicit, comparisons of NNT estimates from different studies should account for the duration of follow-up used to create each estimate. In addition, the NNT concept assumes a homogeneity in response to treatment that may not be accurate. The NNT is simply another way of summarizing the absolute treatment difference and does not provide any unique information.

### CLINICAL PRACTICE GUIDELINES

According to the 1990 Institute of Medicine definition, clinical practice guidelines are “systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances.” This definition emphasizes several crucial features of modern guideline development. First, guidelines are created by using the tools of EBM. In particular, the core of the development process is a systematic literature search followed by a review of the relevant peer-reviewed literature. Second, guidelines usually are focused on a clinical disorder (e.g., diabetes mellitus, stable angina pectoris) or a health care intervention (e.g., cancer screening). Third, the primary objective of guidelines is to improve the quality of medical care by identifying care practices which should be routinely implemented, based on high quality evidence and high benefit to harm ratios for the interventions. Guidelines are intended to “assist” decision-making, not to define explicitly what decisions should be made in a particular situation, in part because guideline level evidence alone is never sufficient for clinical decision-making (e.g., deciding whether to intubate and administer antibiotics for pneumonia in a terminally ill individual, in an individual with dementia, or in an otherwise healthy 30-year-old mother).

Guidelines are narrative documents constructed by expert panels whose composition often is determined by interested professional organizations. These panels vary in expertise and in the degree to which they represent all relevant stakeholders. The guideline documents consist of a series of specific management recommendations, a summary indication of the quantity and quality of evidence supporting each recommendation, an assessment of the benefit to harm ratio for the recommendation, and a narrative discussion of the recommendations. Many recommendations simply reflect the expert consensus of the guideline panel because literature-based evidence is insufficient or absent. The final step in guideline construction is peer review, followed by a final revision in response to the critiques provided. To improve the reliability and trustworthiness of guidelines, the National Academy of Medicine (formerly Institute of Medicine) has made methodological recommendations for guideline development.

Guidelines are closely tied to the process of quality improvement in medicine through their identification of evidence-based best practices. Such practices can be used as quality indicators. Examples include the proportion of acute MI patients who receive aspirin upon admission to a hospital and the proportion of heart failure patients with a depressed ejection fraction treated with an ACE inhibitor.

### CONCLUSIONS

In this era of EBM, it is tempting to think that all the difficult decisions practitioners face have been or soon will be solved and digested into practice guidelines and computerized reminders. However, EBM

provides practitioners with an ideal rather than a finished set of tools with which to manage patients. Moreover, even with such evidence, it is always worth remembering that the response to therapy of the “average” patient represented by the summary clinical trial outcomes may not be what can be expected for the specific patient sitting in front of a provider in the clinic or hospital. In addition, meta-analyses cannot generate evidence when there are no adequate randomized trials, and most of what clinicians confront in practice will never be thoroughly tested in a randomized trial. For the foreseeable future, excellent clinical reasoning skills and experience supplemented by well-designed quantitative tools and a keen appreciation for the role of individual patient preferences in their health care will continue to be of paramount importance in the practice of clinical medicine.

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## 4

## Screening and Prevention of Disease

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A primary goal of health care is to prevent disease or detect it early enough that intervention will be more effective. Tremendous progress has been made toward this goal over the last 50 years. Screening tests are available for many common diseases and encompass biochemical (e.g., cholesterol, glucose), physiologic (e.g., blood pressure, growth curves), radiologic (e.g., mammogram, bone densitometry), and cytologic (e.g., Pap smear) approaches. Effective preventive interventions have resulted in dramatic declines in mortality from many diseases, particularly infections. Preventive interventions include counseling about risk behaviors, vaccinations, medications, and, in some relatively uncommon settings, surgery. Preventive services (including screening tests, preventive interventions, and counseling) are different than other medical interventions because they are proactively administered to healthy individuals instead of in response to a symptom, sign, or diagnosis. Thus, the decision to recommend a screening test or preventive intervention requires a particularly high bar of evidence that testing and intervention are both practical and effective.



Because population-based screening and prevention strategies must be extremely low risk to have an acceptable benefit-to-harm ratio, the ability to target individuals who are more likely to