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Evidence-Based Imaging

Improving the Quality of Imaging in Patient Care

Revised Edition

Springer

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With 264 Illustrations, 20 in Full Color

Foreword by Bruce J. Hillman, MD

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ISBN 978-1-4419-7776-2 e-ISBN 978-1-4419-7777-9
DOI 10.1007/978-1-4419-7777-9
Springer New York Dordrecht Heidelberg London

Library of Congress Control Number: 2011924338

To our patients, who are our best teachers,
and to the researchers, who made this book possible.
To our families, friends, and mentors.

Foreword

Despite our best intentions, most of what constitutes modern medical imaging practice is based on habit, anecdotes, and scientific writings that are too often fraught with biases. Best estimates suggest that only around 30% of what constitutes "imaging knowledge" is substantiated by reliable scientific inquiry. This poses problems for clinicians and radiologists, because inevitably, much of what we do for patients ends up being inefficient, inefficacious, or occasionally even harmful.

In recent years, recognition of how the unsubstantiated practice of medicine can result in poor-quality care and poorer health outcomes has led to a number of initiatives. Most significant in my mind is the evidence-based medicine movement that seeks to improve clinical research and research synthesis as a means of providing a more definitive knowledge basis for medical practice. Although the roots of evidence-based medicine are in fields other than radiology, in recent years, a number of radiologists have emerged to assume leadership roles. Many are represented among the authors and editors of this excellent book, the purpose of which is to enhance understanding of what constitutes the evidence basis for the practice of medical imaging and where that evidence basis is lacking.

It comes not a moment too soon, given how much is going on in the regulatory and payer worlds concerning health care quality. There is a general lack of awareness among radiologists about the insubstantiality of the foundations of our practices. Through years of teaching medical students, radiology residents and fellows, and practicing radiologists in various venues, it occurs to me that at the root of the problem is a lack of sophistication in reading the radiology literature. Many clinicians and radiologists are busy physicians, who, over time, have taken more to reading reviews and scanning abstracts than critically examining the source of practice pronouncements. Even in our most esteemed journals, literature reviews tend to be exhaustive regurgitations of everything that has been written, without providing much insight into which studies were performed more rigorously and hence are more believable. Radiology training programs spend inordinate time cramming the best and brightest young minds with acronyms, imaging "signs," and unsubstantiated factoids while mostly ignoring teaching future radiologists how to think rigorously about what they are reading and hearing.

As I see it, the aim of this book is nothing less than to begin to reverse these conditions. This book is not a traditional radiology text. Rather, the editors and authors have provided first a framework for how to think about many of the most important imaging issues of our day and then fleshed out each chapter with a critical review of the information available in the literature.

There are a number of very appealing things about the approach employed here. First, the chapter authors are a veritable "who's who" of the most thoughtful individuals in our field. Reading this book provides a window into how they think as they evaluate the literature and arrive at their conclusions, which we can use as models for our own improvement. Many of the chapters are coauthored by radiologists and practicing clinicians, allowing for more diverse perspectives. The editors have designed a uniform approach for each chapter and held the authors'

feet to the fire to adhere to it. Chapters 5–40 provide, up front, a summary of the key points. The literature reviews that follow are selective and critical, rating the strength of the literature to provide insight for the critical reader into the degree of confidence he or she might have in reviewing the conclusions. At the end of each chapter, the authors present the imaging approaches that are best supported by the evidence and discuss the gaps that exist in the evidence that should cause us lingering uncertainty. Figures and tables help focus the reader on the most important information, while decision trees provide the potential for more active engagement. Case studies help actualize the main points brought home in each chapter. At the end of each chapter, bullets are used to highlight areas where there are important gaps in research.

The result is a highly approachable text that suits the needs of both the busy practitioner who wants a quick consultation on a patient with whom he or she is actively engaged or the radiologist who wishes a comprehensive, in-depth view of an important topic. Most importantly, from my perspective, the book goes counter to the current trend of "dumbing down" radiology that I abhor in many modern textbooks. To the contrary, this book is an intelligent effort that respects the reader's potential to think for himself or herself and gives substance to Plutarch's famous admonition, "The mind is not a vessel to be filled but a fire to be kindled."

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Preface

All is flux, nothing stays still.
Nothing endures but change.
Heraclitus, 540–480 B.C.

Medical imaging has grown exponentially in the last three decades with the development of many promising and often noninvasive diagnostic studies and therapeutic modalities. The corresponding medical literature has also exploded in volume and can be overwhelming to physicians. In addition, the literature varies in scientific rigor and clinical applicability. The purpose of this book is to employ stringent evidence-based medicine criteria to systematically review the evidence defining the appropriate use of medical imaging and to present to the reader a concise summary of the best medical imaging choices for patient care.

Since our prior version, we have added ten new chapters that cover radiation risk in medical imaging, economic and regulatory impact of evidence-based imaging in the new health care reform environment, and new topics on common disorders. The 40 chapters cover the most prevalent diseases in developed countries, including the four major causes of mortality and morbidity: injury, coronary artery disease, cancer, and cerebrovascular disease. Most of the chapters have been written by radiologists and imagers in close collaboration with clinical physicians and surgeons to provide a balanced and fair analysis of the different medical topics. In addition, we address in detail both the adult and pediatric sides of the issues. We cannot answer all questions – medical imaging is a delicate balance of science and art, often without data for guidance – but we can empower the reader with the current evidence behind medical imaging.

To make the book user-friendly and to enable fast access to pertinent information, we have organized all of the chapters in the same format. The chapters are framed around important and provocative clinical questions relevant to the daily physician's practice. A short listing of issues at the beginning of each chapter helps three different tiers of users: (1) the busy physician searching for quick guidance, (2) the meticulous physician seeking deeper understanding, and (3) the medical-imaging researcher requiring a comprehensive resource. Key points and summarized answers to the important clinical issues are at the beginning of the chapters, so the busy clinician can understand the most important evidence-based imaging data in seconds. Each important question and summary is followed by a detailed discussion of the supporting evidence so that the meticulous physician can have a clear understanding of the science behind the evidence.

In each chapter, the evidence discussed is presented in tables and figures that provide an easy review in the form of summary tables and flow charts. The imaging case series highlights the strengths and limitations of the different imaging studies with vivid examples. Toward the end of the chapters, the best imaging protocols are described to ensure that the imaging studies are well standardized and done with the highest available quality. The final section of the chapters is Future Research, in which provocative questions are raised for physicians and nonphysicians interested in advancing medical imaging.

Not all research and not all evidence are created equal. Accordingly, throughout the book, we use a four-level classification detailing the strength of the evidence and based on the Oxford-criteria: level I (strong evidence), level II (moderate evidence), level III (limited evidence), and level IV (insufficient evidence). The strength of the evidence is presented in parenthesis throughout the chapter so the reader gets immediate feedback on the weight of the evidence behind each topic.

Finally, we had the privilege of working with a group of outstanding contributors from major medical centers and universities in North America and Europe. We believe that the authors' expertise, breadth of knowledge, and thoroughness in writing the chapters provide a valuable source of information and can guide decision-making for physicians and patients. In addition to guiding practice, the evidence summarized in the chapters may have policy-making and public health implications. We hope that the book highlights key points and generates discussion, promoting new ideas for future research. Finally, regardless of the endless hours spent researching the multiple topics in-depth, evidence-based imaging remains a work in progress. We value your suggestions and comments on how to improve this book. Please email them to us, so we can bring you the best of the evidence over the years.

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Part I

Principles, Methodology, Economics, and Radiation Risk

1

Principles of Evidence-Based Imaging

L. Santiago Medina, C. Craig Blackmore, and Kimberly E. Applegate

Medicine is a science of uncertainty and an art of probability.

Sir William Osler

Issues

I. What Is Evidence-Based Imaging?

The standard medical education in Western medicine has emphasized skills and knowledge learned from experts, particularly those encountered in the course of postgraduate medical education, and through national publications and meetings. This reliance on experts, referred to by Dr. Paul Gerber of Dartmouth Medical School as "eminence-based medicine" (1), is based on the construct that the individual practitioner, particularly a specialist devoting extensive time to a given discipline, can arrive at the best approach to a problem through his or her experience. The practitioner builds up an experience base over years and digests information from national experts who have a greater base of experience due to their focus in a particular area. The evidence-based imaging (EBI) paradigm, in contradistinction, is based

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L.S. Medina et al. (eds.), *Evidence-Based Imaging: Improving the Quality of Imaging in Patient Care, Revised Edition*,
DOI 10.1007/978-1-4419-7777-9_1,

on the precept that a single practitioner cannot through experience alone arrive at an unbiased assessment of the best course of action. Assessment of appropriate medical care should instead be derived through evidence-based process. The role of the practitioner, then, is not simply to accept information from an expert, but rather to assimilate and critically assess the research evidence that exists in the literature to guide a clinical decision (2–4).

Fundamental to the adoption of the principles of EBI is the understanding that medical care is not optimal. The life expectancy at birth in the United States for males and females in 2005 was 75 and 80 years, respectively (Table 1.1). This is slightly lower than the life expectancies in other industrialized nations such as the United Kingdom and Australia (Table 1.1). In fact, the World Health Organization ranks the USA 50th in life expectancy and 72nd in overall health. The United States spent at least 15.2% of the gross domestic product (GDP) in order to achieve this life expectancy. This was significantly more than the United Kingdom and Australia, which spent about half that (Table 1.1). In addition, the US per capita health expenditure was $6,096, which was twice the expenditure in the United Kingdom or Australia. In conclusion, the United States spends significantly more money and resources than other industrialized countries to achieve a similar outcome in life expectancy. This implies that a significant amount of resources is wasted in the US health care system. In 2007, the United States spent $2.3 trillion in health care or 16% of its GDP. By 2016, the US health percent of the GDP is expected to grow to 20% or $4.2 trillion (5). Recent estimates prepared by the Commonwealth Fund Commission (USA) on a High Performance Health System indicate that $1.5 trillion could be saved over a 10-year period if a combination of options, including evidence-based medicine and universal health insurance, was adopted (6).

Simultaneous with the increase in health care costs has been an explosion in available medical information. The National Library of Medicine PubMed search engine now lists over 18 million citations. Practitioners cannot maintain familiarity with even a minute subset of this literature without a method of filtering out publications that lack appropriate methodological quality. EBI is a promising method of identifying appropriate information to guide practice and to improve the efficiency and effectiveness of imaging.

Evidence-based imaging is defined as medical decision making based on clinical integration of the best medical imaging research evidence with the physician's expertise and with patient's expectations (2–4). The best medical imaging research evidence often comes from the basic sciences of medicine. In EBI, however, the basic science knowledge has been translated into patient-centered clinical research, which determines the accuracy and role of diagnostic and therapeutic imaging in patient care (3). New evidence may make current diagnostic tests obsolete and new ones more accurate, less invasive, safer, and less costly (3). The physician's expertise entails the ability to use the referring physician's clinical skills and

Table 1.1. Life expectancy and health care spending in three developed countries

	Life expectancy at birth (2005)		Percentage of GDP in health care (2007) (%)	Per capita health expenditure (2007)
	Male	Female		
United States	**75.3**	**80.3**	**16.0**	**$6,096**
United Kingdom	**77.4**	**81.4**	**8.3**	**$2,560**
Australia	**79.5**	**84.5**	**9.1**	**$3,123**

Sources: United Kingdom Office of National Statistics; Australian Bureau of Statistics; Per capita expenditures: *Human Development Report, 2007*, United Nations, hdr.undp.org; Life expectancy: Kaiser Family Foundation web site with stated source: WHO, World Health Statistics 2007, available at: http://www.who.int/whosis/en/.

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GDP gross domestic product.

past experience to rapidly identify high-risk individuals who will benefit from the diagnostic information of an imaging test (4). Patient's expectations are important because each individual has values and preferences that should be integrated into the clinical decision making in order to serve our patients' best interests (3). When these three components of medicine come together, clinicians and imagers form a diagnostic team, which will optimize clinical outcomes and quality of life for our patients.

II. The Evidence-Based Imaging Process

The EBI process involves a series of steps: (A) formulation of the clinical question, (B) identification of the medical literature, (C) assessment of the literature, (D) summary of the evidence, and (E) application of the evidence to derive an appropriate clinical action. This book is designed to bring the EBI process to the clinician and imager in a user-friendly way. This introductory chapter details each of the steps in the EBI process. Chapter 2 discusses how to critically assess the literature. The rest of the book makes available to practitioners the EBI approach to numerous key medical imaging issues. Each chapter addresses common pediatric disorders ranging from congenital anomalies to asthma to appendicitis. Relevant clinical questions are delineated, and then each chapter discusses the results of the critical analysis of the identified literature. The results of this analysis are presented with meta-analyses where appropriate. Finally, we provide simple recommendations for the various clinical questions, including the strength of the evidence that supports these recommendations.

A. Formulating the Clinical Question

The first step in the EBI process is formulation of the clinical question. The entire process of EBI arises from a question that is asked in the context of clinical practice. However, often formulating a question for the EBI approach can be more challenging than one would believe intuitively. To be approachable by the EBI format, a question must be specific to a clinical situation, a patient group, and an outcome or action. For example, it would not be appropriate to simply ask which imaging technique is better – computed tomography (CT) or radiography. The question must be refined to include the particular patient population and the action that the imaging will be used to direct. One can refine the question to include a particular population (which imaging technique is better in pediatric victims of high-energy blunt trauma) and to guide a particular action or decision (to exclude the presence of unstable cervical spine fracture). The full EBI question then becomes, in pediatric victims of high-energy blunt trauma, which imaging modality is preferred, CT or radiography, to exclude the presence of unstable cervical spine fracture? This book addresses questions that commonly arise when employing an EBI approach for the care of children and adolescents. These questions and issues are detailed at the start of each chapter.

B. Identifying the Medical Literature

The process of EBI requires timely access to the relevant medical literature to answer the question. Fortunately, massive on-line bibliographical references such as PubMed are available. In general, titles, indexing terms, abstracts, and often the complete text of much of the world's medical literature are available through these on-line sources. Also, medical librarians are a potential resource to aid identification of the relevant imaging literature. A limitation of today's literature data sources is that often too much information is available and too many potential resources are identified in a literature search. There are currently over 50 radiology journals, and imaging research is also frequently published in journals from other medical subspecialties. We are often confronted with more literature and information than we can process. The greater challenge is to sift through the literature that is identified to select that which is appropriate.

C. Assessing the Literature

To incorporate evidence into practice, the clinician must be able to understand the published literature and to critically evaluate the strength of the evidence. In this introductory chapter on

the process of EBI, we focus on discussing types of research studies. Chapter 2 is a detailed discussion of the issues in determining the validity and reliability of the reported results.

1. What Are the Types of Clinical Studies?

An initial assessment of the literature begins with determination of the type of clinical study: descriptive, analytical, or experimental (7). *Descriptive* studies are the most rudimentary, as they only summarize disease processes as seen by imaging, or discuss how an imaging modality can be used to create images. Descriptive studies include case reports and case series. Although they may provide important information that leads to further investigation, descriptive studies are not usually the basis for EBI.

Analytic or *observational* studies include cohort, case–control, and cross-sectional studies (Table 1.2). Cohort studies are defined by risk factor status, and case–control studies consist of groups defined by disease status (8). Both case–control and cohort studies may be used to define the association between an intervention, such as an imaging test, and patient outcome (9). In a cross-sectional (prevalence) study, the researcher makes all of his measurements on a single occasion. The investigator draws a sample from the population (i.e., asthma in 5- to 15-year-olds) and determines distribution of variables within that sample (7). The structure of a cross-sectional study is similar to that of a cohort study except that all pertinent measurements (i.e., PFTs) are made at once, without a follow-up period. Cross-sectional studies can be used as a major source for health and habits of different populations and countries, providing estimates of such parameters as the prevalence of asthma, obesity, and congenital anomalies (7, 10).

In *experimental studies* or *clinical trials*, a specific intervention is performed and the effect of the intervention is measured by using a control group (Table 1.2). The control group may be tested with a different diagnostic test and treated with a placebo or an alternative mode of therapy (7, 11). Clinical trials are epidemiologic designs that can provide data of high quality that resemble the controlled experiments done by basic science investigators (8). For example, clinical trials may be used to assess new diagnostic tests (e.g., high-resolution CT for cystic fibrosis) or new interventional procedures (e.g., stenting for coronary artery anomalies).

Studies are also traditionally divided into retrospective and prospective (Table 1.2) (7, 11). These terms refer more to the way the data are gathered than to the specific type of study design. In *retrospective studies*, the events of interest have occurred before study onset. Retrospective studies are usually done to assess rare disorders, for pilot studies, and when prospective investigations are not possible. If the disease process is considered rare, retrospective studies facilitate the collection of enough subjects to have meaningful data. For a pilot project, retrospective studies facilitate the collection of preliminary data that can be used to improve the study design in future prospective studies. The major drawback of a retrospective study is incomplete data acquisition (10). Case–control studies are usually retrospective. For example, in a case–control study, subjects in the case group (patients with perforated appendicitis) are compared with subjects in a control group (nonperforated appendicitis) to determine factors associated with perforation (e.g., duration of symptoms, presence of appendicolith, size of appendix) (10).

Table 1.2. Study design

	Prospective follow-up	Randomization of subjects	Controls
Case report or series	**No**	**No**	**No**
Cross-sectional study	**No**	**No**	**Yes**
Case–control study	**No**	**No**	**Yes**
Cohort study	**Yes/no**	**No**	**Yes**
Randomized controlled trial	**Yes**	**Yes**	**Yes**

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In *prospective studies*, the event of interest transpires after study onset. Prospective studies, therefore, are the preferred mode of study design, as they facilitate better control of the design and the quality of the data acquired (7). Prospective studies, even large studies, can be performed efficiently and in a timely fashion if done on common diseases at major institutions, as multicenter trials with adequate study populations (12). The major drawback of a prospective study is the need to make sure that the institution and personnel comply with strict rules concerning consents, protocols, and data acquisition (11). Persistence, to the point of irritation, is crucial to completing a prospective study. Cohort studies and clinical trials are usually prospective. For example, a cohort study could be performed in children with splenic injury in which the risk factor of presence of arterial blush is correlated with the outcome of failure of nonmedical management, as the patients are followed prospectively over time (10).

The strongest study design is the prospective randomized, blinded clinical trial (Table 1.2) (7). The randomization process helps to distribute known and unknown confounding factors, and blinding helps to prevent observer bias from affecting the results (7, 8). However, there are often circumstances in which it is not ethical or practical to randomize and follow patients prospectively. This is particularly true in rare conditions, and in studies to determine causes or predictors of a particular condition (9). Finally, randomized clinical trials are expensive and may require many years of follow-up. Not surprisingly, randomized clinical trials are uncommon in radiology. The evidence that supports much of radiology practice is derived from cohort and other observational studies. More randomized clinical trials are necessary in radiology to provide sound data to use for EBI practice (3).

2. *What Is the Diagnostic Performance of a Test: Sensitivity, Specificity, and Receiver Operating Characteristic Curve?*

Defining the presence or absence of an outcome (i.e., disease and nondisease) is based on a standard of reference (Table 1.3). While a perfect standard of reference or so-called gold standard can never be obtained, careful attention should be paid to the selection of the standard that should be widely believed to offer the best approximation to the truth (13).

In evaluating diagnostic tests, we rely on the statistical calculations of sensitivity and specificity (see Appendix 1). Sensitivity and specificity of a diagnostic test are based on the two-way (2 × 2) table (Table 1.3). Sensitivity refers to the proportion of subjects with the disease who have a positive test and is referred to as the true positive rate (Fig. 1.1). Sensitivity, therefore, indicates how well a test identifies the subjects with disease (7, 14).

Table 1.3. Two-way table of diagnostic testing

	Disease (gold standard)	
Test result	**Present**	**Absent**
Positive	**a (TP)**	**b (FP)**
Negative	**c (FN)**	**d (TN)**

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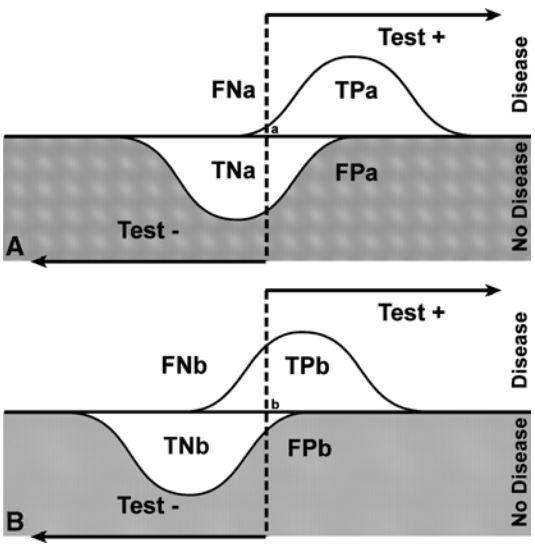

Figure 1.1. Test with a low (**A**) and high (**B**) threshold. The sensitivity and specificity of a test change according to the threshold selected; hence, these diagnostic performance parameters are threshold dependent. Sensitivity with low threshold (TPa/diseased patients) is greater than sensitivity with a higher threshold (TPb/diseased patients). Specificity with a low threshold (TNa/nondiseased patients) is less than specificity with a high threshold (TNb/nondiseased patients). FN false negative; FP false positive; TN true negative; TP true positive. (Reprinted with permission of the American Society of Neuroradiology from Medina (11).)

Specificity is defined as the proportion of subjects without the disease who have a negative index test (Fig. 1.1) and is referred to as the true negative rate. Specificity, therefore, indicates how well a test identifies the subjects with no disease (7, 11). It is important to note that the sensitivity and specificity are characteristics of the test being evaluated and are therefore usually independent of the prevalence (proportion of individuals in a population who have disease at a specific instant) because the sensitivity only deals with the diseased subjects, whereas the specificity only deals with the nondiseased subjects. However, sensitivity and specificity both depend on a threshold point for considering a test positive and hence may change according to which threshold is selected in the study (11, 14, 15) (Fig. 1.1A). Excellent diagnostic tests have high values (close to 1.0) for both sensitivity and specificity. Given exactly the same diagnostic test, and exactly the same subjects confirmed with the same reference test, the sensitivity with a low threshold is greater than the sensitivity with a high threshold. Conversely, the specificity with a low threshold is less than the specificity with a high threshold (Fig. 1.1B) (14, 15).

The effect of threshold on the ability of a test to discriminate between disease and nondisease can be measured by a receiver operating characteristic (ROC) curve (11, 15). The ROC curve is used to indicate the trade-offs between sensitivity and specificity for a particular diagnostic test and hence describes the discrimination capacity of that test. An ROC graph shows the relationship between sensitivity (y axis) and 1 – specificity (x axis) plotted for various cutoff points. If the threshold for sensitivity and specificity are varied, an ROC curve can be generated. The diagnostic performance of a test can be estimated by the area under the ROC curve. The steeper the ROC curve, the greater the area and the better the discrimination of the test (Fig. 1.2). A test with perfect discrimination has an area of 1.0, whereas a test with only random discrimination has an area of 0.5 (Fig. 1.2). The area under the ROC curve usually determines the overall diagnostic performance of the test independent of the threshold selected (11, 15). The ROC curve is threshold independent because it is generated by using varied thresholds of sensitivity and specificity. Therefore, when evaluating a new imaging test, in addition to the sensitivity and specificity, an ROC curve analysis should be

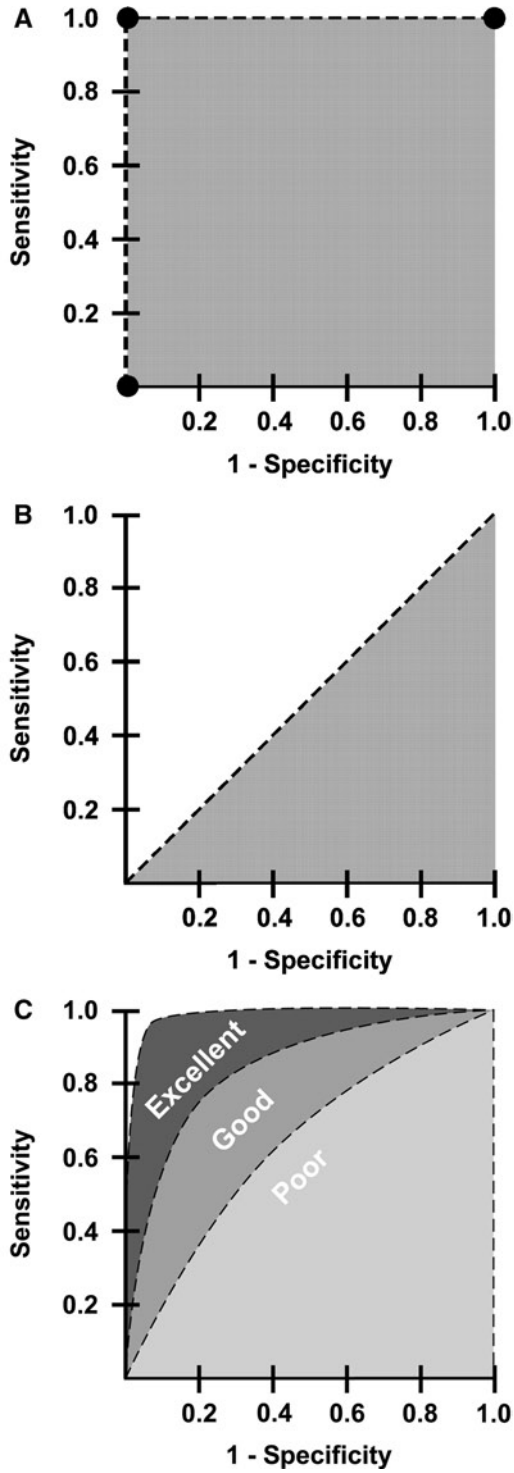

Figure 1.2. The perfect test (**A**) has an area under the curve (AUC) of 1. The useless test (**B**) has an AUC of 0.5. The typical test (**C**) has an AUC between 0.5 and 1. The greater the AUC (i.e., excellent > good > poor), the better the diagnostic performance. (Reprinted with permission of the American Society of Neuroradiology from Medina (11).)

done so that the threshold-dependent and threshold-independent diagnostic performance can be fully determined (10).

3. *What Are Cost-Effectiveness and Cost-Utility Studies?*

Cost-effectiveness analysis (CEA) is an objective scientific technique used to assess alternative health care strategies on both cost and effectiveness (16–18). It can be used to develop clinical and imaging practice guidelines and to set health policy (19). However, it is not designed to be the final answer to the decision-making process; rather, it provides a detailed analysis of the cost and outcome variables and how they are affected by competing medical and diagnostic choices.

Health dollars are limited regardless of the country's economic status. Hence, medical decision makers must weigh the benefits of a diagnostic test (or any intervention) in relation to its cost. Health care resources should be allocated so the maximum health care benefit for the entire population is achieved (10). Cost-effectiveness analysis is an important tool to address health cost-outcome issues in a cost-conscious society. Countries such as Australia usually require robust CEA before drugs are approved for national use (10).

Unfortunately, the term *cost-effectiveness* is often misused in the medical literature (20). To say that a diagnostic test is truly cost-effective, a comprehensive analysis of the entire short- and long-term outcomes and costs needs to be considered. Cost-effectiveness analysis is an objective technique used to determine which of the available tests or treatments are worth the additional costs (21).

There are established guidelines for conducting robust CEA. The US Public Health Service formed a panel of experts on cost-effectiveness in health and medicine to create detailed standards for cost-effectiveness analysis. The panel's recommendations were published as a book in 1996 (21).

D. Types of Economic Analyses in Medicine

There are four well-defined types of economic evaluations in medicine: cost-minimization studies, cost–benefit analyses, cost-effectiveness analyses, and cost-utility analyses. They are all commonly lumped under the term *cost-effectiveness analysis*. However, significant differences exist among these different studies.

Cost-minimization analysis is a comparison of the cost of different health care strategies that are assumed to have identical or similar effectiveness (16). In medical practice, few diagnostic tests or treatments have identical or similar effectiveness. Therefore, relatively few articles have been published in the literature with this type of study design (22). For example, a recent study demonstrated that functional magnetic resonance imaging (MRI) and the Wada test have similar effectiveness for language lateralization, but the later is 3.7 times more costly than the former (23).

Cost–benefit analysis (CBA) uses monetary units such as dollars or euros to compare the costs of a health intervention with its health benefits (16). It converts all benefits to a cost equivalent and is commonly used in the financial world where the cost and benefits of multiple industries can be changed to only monetary values. One method of converting health outcomes into dollars is through a contingent valuation or willingness-to-pay approach. Using this technique, subjects are asked how much money they would be willing to spend to obtain, or avoid, a health outcome. For example, a study by Appel et al. (24) found that individuals would be willing to pay $50 for low osmolar contrast agents to decrease the probability of side effects from intravenous contrast. However, in general, health outcomes and benefits are difficult to transform to monetary units; hence, CBA has had limited acceptance and use in medicine and diagnostic imaging (16, 25).

Cost-effectiveness analysis (CEA) refers to analyses that study both the effectiveness and cost of competing diagnostic or treatment strategies, where effectiveness is an objective measure (e.g., intermediate outcome: number of strokes detected; or long-term outcome: life-years saved). Radiology CEAs often use intermediate outcomes, such as lesion identified, length of stay, and number of avoidable surgeries (16, 18). However, ideally, long-term outcomes such as life-years saved (LYS) should be used (21). By using LYS, different health care fields or interventions can be compared.

Cost-utility analysis is similar to CEA except that the effectiveness also accounts for quality of life issues. Quality of life is measured as utilities that are based on patient preferences (16).

The most commonly used utility measurement is the quality-adjusted life year (QALY). The rationale behind this concept is that the QALY of excellent health is more desirable than the same 1 year with substantial morbidity. The QALY model uses preferences with weight for each health state on a scale from 0 to 1, where 0 is death and 1 is perfect health. The utility score for each health state is multiplied by the length of time the patient spends in that specific health state (16, 26). For example, let us assume that a patient with a congenital heart anomaly has a utility of 0.8 and he spends 1 year in this health state. The patient with the cardiac anomaly would have a 0.8 QALY in comparison with his neighbor who has a perfect health and hence a 1 QALY.

Cost-utility analysis incorporates the patient's subjective value of the risk, discomfort, and pain into the effectiveness measurements of the different diagnostic or therapeutic alternatives. In the end, all medical decisions should reflect the patient's values and priorities (26). That is the explanation of why cost-utility analysis is becoming the preferred method for evaluation of economic issues in health (19, 21). For example, in low-risk newborns with intergluteal dimple suspected of having occult spinal dysraphism, ultrasound was the most effective strategy with an incremented cost-effectiveness ratio of $55,100 per QALY. In intermediate-risk newborns with low anorectal malformation, however, MRI was more effective than ultrasound at an incremental cost-effectiveness of $1,000 per QALY (27).

Assessment of Outcomes: The major challenge to cost-utility analysis is the quantification of health or quality of life. One way to quantify health is descriptive analyses. By assessing what patients can and cannot do, how they feel, their mental state, their functional independence, their freedom from pain, and any number of other facets of health and well-being that are referred to as domains, one can summarize their overall health status. Instruments designed to measure these domains are called health status instruments. A large number of health status instruments exist, both general instruments, such as the SF-36 (28), and instruments that are specific to particular disease states, such as the Roland scale for back pain. These various scales enable the quantification of health benefit. For example, Jarvik et al. (29) found no significant difference in the Roland score between patients randomized to MRI versus radiography for low back pain, suggesting that MRI was not worth the additional cost. There are additional issues in applying such tools to children, as they may be too young to understand the questions being asked. Parents can sometimes be used as surrogates, but parents may have different values and may not understand the health condition from the perspective of the child.

Assessment of Cost: All forms of economic analysis require assessment of cost. However, assessment of cost in medical care can be confusing, as the term *cost* is used to refer to many different things. The use of charges for any sort of cost estimation, however, is inappropriate. Charges are arbitrary and have no meaningful use. Reimbursements, derived from Medicare and other fee schedules, are useful as an estimation of the amounts society pays for particular health care interventions. For an analysis taken from the societal perspective, such reimbursements may be most appropriate. For analyses from the institutional perspective or in situations where there are no meaningful Medicare reimbursements, assessment of actual direct and overhead costs may be appropriate (30).

Direct cost assessment centers on the determination of the resources that are consumed in the process of performing a given imaging study, including *fixed costs* such as equipment and *variable costs* such as labor and supplies. Cost analysis often utilizes activity-based costing and time motion studies to determine the resources consumed for a single intervention in the context of the complex health care delivery system. *Overhead*, or *indirect cost*, assessment includes the costs of buildings, overall administration, taxes, and maintenance that cannot be easily assigned to one particular imaging study. Institutional cost accounting systems may be used to determine both the direct costs of an imaging study and the amount of institutional overhead costs that should be apportioned to that particular test. For example, Medina et al. (31) in a vesicoureteral reflux imaging study in children with urinary tract infection found a significant difference ($p < 0.0001$) between the mean total direct cost of voiding cystourethrography ($112.7 ± $10.33) and radionuclide cystography ($64.58 ± $1.91).