Published in final edited form as:

Am J Bioeth. 2009 April ; 9(4): 3–14. doi:10.1080/15265160902790583.

Screening in the Dark: Ethical Considerations of Providing Screening Tests to Individuals When Evidence is Insufficient to Support Screening Populations

Ingrid M. Burger and

Johns Hopkins Bloomberg School of Public Health

Nancy E. Kass

Johns Hopkins Bloomberg School of Public Health, and Berman Institute of Bioethics, Johns Hopkins University

Abstract

During the past decade, screening tests using computed tomography (CT) have disseminated into practice and been marketed to patients despite neither conclusive evidence nor professional agreement about their efficacy and cost-effectiveness at the population level. This phenomenon raises questions about physicians' professional roles and responsibilities within the setting of medical innovation, as well as the appropriate scope of patient autonomy and access to unproven screening technology. This article explores how physicians ought to respond when new screening examinations that lack conclusive evidence of overall population benefit emerge in the marketplace and are requested by individual patients. To this end, the article considers the nature of evidence and how it influences decision-making for screening at both the public policy and individual patient levels. We distinguish medical and ethical differences between screening recommended for a population and screening considered on an individual patient basis. Finally, we discuss specific cases to explore how evidence, patient risk factors and preferences, and physician judgment ought to balance when making individual patient screening decisions.

Keywords

computed tomography; decision-making; evidence; ethics; professionalism; screening

During the past decade, screening tests using computed tomography (CT) have disseminated into practice despite neither conclusive evidence nor professional agreement about their efficacy and cost-effectiveness at the population level (United States Preventive Services Task Force [US PSTF] 2004a; Hillman 2003a; Illes et al. 2003; Kalish et al. 2004; Lee and Brennan 2002; American College of Radiology [ACR] 2004). These screening tests often involve CT scans that aim to detect specific diseases, such as chest CT to detect lung cancer

Copyright © Taylor & Francis Group, LLC

Address correspondence to Ingrid M. Burger, University of California, San Francisco, Department of Radiology, 505 Parnassus Ave., M-391, San Francisco, CA 94143-0628. ingrid.burger@gmail.com.

Publisher's Disclaimer: Full terms and conditions of use: <http://www.informaworld.com/terms-and-conditions-of-access.pdf>

This article may be used for research, teaching and private study purposes. Any substantial or systematic reproduction, re-distribution, re-selling, loan or sub-licensing, systematic supply or distribution in any form to anyone is expressly forbidden.

The publisher does not give any warranty express or implied or make any representation that the contents will be complete or accurate or up to date. The accuracy of any instructions, formulae and drug doses should be independently verified with primary sources. The publisher shall not be liable for any loss, actions, claims, proceedings, demand or costs or damages whatsoever or howsoever caused arising directly or indirectly in connection with or arising out of the use of this material.

in smokers or CT angiography to detect cerebral aneurysms. Additionally, whole-body CT screening examinations aim to search for a wide range of possible diseases. Screening CT tests are directed at apparently healthy adults, who may have risk factors such as smoking or family history, to detect disease that has not yet produced symptoms. The hope is that by detecting such diseases at earlier stages, patient outcomes will improve and treatment will be less costly than if detected at a later stage.

The primary goal of population-based screening is to decrease disease-specific mortality (Black & Welch 1997; Kopans et al. 2003; Morrison 1992). Most CT screening tests lack sufficient evidence demonstrating reduction in population mortality and are not recommended by professional societies as population-based screening tools (Administration 2002; Council on Scientific Affairs 2003; Force 2004a; Radiology 2004). Nevertheless, many individual physicians and physician groups offer a variety of screening tests, at times marketing screening services directly to consumers (Illes et al. 2004). Indeed, patients generally seek these tests themselves and, in certain instances, obtain screening tests without a physician's referral ("patient self-referral").

In an era that promotes evidence-based medicine and cost effectiveness, the marketing and diffusion of these CT screening examinations into current practice before rigorous empirical evaluation raises concern. Image-based screening tests carry important risks for patients: CT exposes patients to radiation, and high false positive rates may lead to invasive, risky, and costly follow-up procedures. Further, the detection of pseudo-disease—that is, cancers that grow so slowly that they never produce symptoms or impact a patient's health—leads to interventions and treatments that provide no medical benefit and may pose significant risk (Black and Welch 1993; Malm 1999; Welch 1996, 2001, 2004). Those supporting widely available CT screening, however, argue that the benefits of early detection outweigh these risks. Supporters also consider that patients ought to have access to new screening technology in the pursuit of preventive healthcare, either with or without a physician's referral, and should be able to decide for themselves if the benefits outweigh the risks without waiting several years for the results of rigorous efficacy studies (Brant-Zawadzki 2000, 2002a; Henschke et al. 2006; Siedt 2004).

The early diffusion of CT screening tests into practice raises questions about physicians' professional roles and responsibilities within the setting of medical innovation, as well as the appropriate scope of patient autonomy and access to unproven medical technology. The purpose of this article is to explore how physicians ought to respond when new screening examinations that lack conclusive evidence of overall population benefit emerge in the marketplace and are requested by individual patients. To this end, the article begins by considering the nature of evidence and how it influences decision-making for screening at both the public policy level and at the level of the individual physician and patient. We distinguish important medical and ethical differences between screening that is recommended for a population, and screening that may be considered on an individual-patient basis when population screening is not yet recommended. Finally, we discuss several specific cases in order to explore how evidence, patient risk factors and preferences, and physician judgment ought to balance when making individual patient screening decisions. We shall argue that under most circumstances, physicians should discourage individual patient access to screening examinations prior to conclusive evidence and professional society endorsement of population-based screening. However, there may be certain circumstances under which it could be appropriate to screen patients, provided that well-controlled observational studies have established the possibility of early detection, patients have well-defined risk factors for the screened disease, patients greatly value screening information, and physicians believe the benefits may outweigh the risks for particular patients.

While our discussion will focus on the diffusion of CT screening tests, many of the issues raised by these particular tests can be generalized to other areas of medicine where new technology is introduced and marketed to patients before conclusive evidence and professional agreement exist about its benefit to populations.

THE ROLES AND LIMITATIONS OF EVIDENCE IN GUIDING DECISION-MAKING

Traditional principles of medical ethics, including beneficence, autonomy, and justice (Beauchamp and Childress 2000), help articulate the moral force of grounding treatment decisions in evidence. Ashcroft (2004) writes that advocates of evidence-based medicine (EBM):

can generally be characterized as having a strong ethical sense of the importance of avoiding unnecessary harms to patients and improving health care in the interests of the general good ... This approach had a strong ethical imperative behind it, rooted in concern to do no harm, to do one's best for one's patient, and to do so justly by eliminating waste (131).

Physicians are entrusted with promoting the well-being of patients by recommending treatments that are on balance beneficial. Proponents of EBM assert that only well-designed clinical trials can quantify the risks and benefits of certain treatments to a level of sufficient accuracy, enabling physicians and patients to understand and choose the best course of treatment. Further, evidence regarding the outcomes of treatments applied to well-defined groups of patients can guide policy makers in their efforts to optimally allocate resources, in turn improving distributive justice in the healthcare system.

While there are strong ethical reasons to ground both health policy decisions and individual patient care decisions in evidence, great variability exists in the strength of evidence for tests and therapies in medicine. The traditional "levels of evidence" in EBM, ranging lowest to highest, include expert opinion, single case reports, uncontrolled case series, case series using historical controls, controlled observational studies, and finally randomized controlled trials (RCTs) (Cochrane.org; Meakins 2002). For screening tests, the level of evidence produced by particular study designs has important implications for screening decisions. For example, observational studies, namely case-control or cohort studies, that control for relevant variables in the screened and non-screened groups may reliably demonstrate that a screening test detects disease at an earlier stage. Importantly, however, increased detection of early-stage cancers and prolonged survival represent intermediate endpoints that may not translate into improved morbidity and mortality for the screened population.¹ Observational designs are subject to the effects of lead time, length time, and overdiagnosis biases, and cannot answer the question of whether or not screening improves overall population outcomes, such as disease-specific mortality, considered to be a more important endpoint. (Black and Welch 1997).

RCTs are considered the highest level of clinical evidence (Pocock 1983), and are of particular importance for evaluating screening tests; RCT designs avoid important biases and can provide valid information about whether improves disease-specific mortality in the screened population (Black and Welch 1997) The value of RCTs has been demonstrated via numerous examples in recent history of procedures and devices that were developed and disseminated into practice, only later to be shown in randomized clinical trials to be

¹*Disease-specific survival and disease-specific mortality* are distinct ideas, measured in different ways. Survival statistics are better suited to measuring patient outcomes after treatment of known disease, whereas mortality is better suited to measuring the outcomes of population screening; unlike survival statistics, mortality measurements are resistant to the biases described previously in text.

ineffective or harmful (Cobb et al. 1959; Dimond et al. 1960; Group 1985; Mello and Brennan 2001). Unfortunately, RCTs of screening tests can require thousands of patients, years of follow-up, and high cost to complete. A recent example is the National Lung Screening Trial (NLST), sponsored by the National Cancer Institute (Bethesda, MD), to evaluate the benefit of screening smokers for lung cancer with chest CT. The NLST has enrolled 50,000 patients, will take a total of 8 years to complete, and costs approximately \$200 million (Black et al. 2006; Hillman 2003b; Sunshine and Applegate 2004; Swensen et al. 2005). As such, it is not practically feasible to conduct an RCT to evaluate every new screening test.

The level of evidence for various tests or therapies influences the strength and nature of policy recommendations, including population-screening guidelines. For example, the US PSTF and the Physician's Data Query (PDQ) database program have both developed methods for evaluating the scientific evidence behind various preventive medical services, such as screening tests (Franco et al. 2002). The US PTF formulates recommendations of variable strengths depending on the grade, or quality, of evidence, and its recommendations are considered the "gold standard" for preventive services such as screening (Harris et al. 2001; Woloshin et al. 2005; Woolf et al. 1996). According to the US PSTF model, a screening test for which well-designed RCTs demonstrate population benefit, i.e., "level I evidence," may translate to a "grade A" recommendation that there is strong evidence to support screening. Similarly, a screening test for which there are well-designed observational studies, such as a non-randomized cohort or case-control studies, i.e., "level II evidence," may translate into a "grade B" or "grade I" recommendation that there is either fair or insufficient evidence, respectively, to support the test (US PST 2007a; Harris et al. 2001).

While these formalized connections between evidence and clinical guidelines/health policy exist, a subset of physicians and entrepreneurs have marketed CT screening tests directly to consumers before higher-level evidence and professional endorsement exist. This phenomenon raises deeper questions about how evidence ought to play a role in two types of decision-making regarding screening: 1) public policy decisions and practice guidelines to recommend screening for a particular population, and 2) individual decisions between a physician and patient regarding screening. To this end, we shall explore the medical and moral differences between screening activities that are recommended for specific populations, such as mammography for women older than 50 years, and those that have not been recommended for populations but are nonetheless marketed to or requested by individual patients, such as lung CT screening in smokers. The following paragraphs articulate these differences and explain why they may allow different evidence requirements.

Population-Based Screening: Epidemiological Characteristics, Ethical Foundations, Evidence Requirements

Population-based screening is a public health activity. Morrison (1992) has defined population screening as:

a systematic testing of asymptomatic individuals for preclinical disease. The purpose is to prevent or delay the development of advanced disease in the subset of patients with preclinical disease through early detection and treatment (4).

Cole and Morrison (1980) further specified the objective of cancer screening as "to reduce morbidity and mortality from that cancer among persons screened at a reasonable cost" (1263). Most population-based screening tests possess certain defining features: a disease or risk factor to be detected, a specific population screened, a recommended time interval between screening tests, the sensitivity and specificity of the screening test, and the body of

research evidence concerning the medical benefit and cost-effectiveness of screening (Black and Welch 1997; Morrison 1992). Obuchowski and colleagues (2001) have outlined ten criteria for effective screening that can be used to evaluate the utility and appropriateness of an image-based screening test for a population (Table 1).

Population-based screening tests are typically endorsed by professional societies and governmental bodies, such as the American Cancer Society (Atlanta, GA), the American College of Radiology (Reston, VA), and the US PSTF among others, based upon evidence suggesting that the overall benefits to the target population outweigh the risks (US PSTF 2004; Hillman 2003b). Pap smears, mammograms, and colonoscopies are current examples of screening tests recommended for particular target populations. Given the great investment of public resources for promoting a population-based screening examination and its widespread impact on the public's health, the level of evidence required to support population-based screening should be high, ideally based upon RCT data.² Furthermore, Woolf and colleagues (1996) has noted,

the burden of proof [to demonstrate that interventions result in more good than harm before recommending them to the public] is even more appropriate for preventive services [including screening examinations], which are offered to essentially healthy persons as something “good for them” (514).

Once a screening test is recommended, patient and professional groups advocate for insurance coverage in order to provide broader access to screening, based upon the understanding that all in the target population are entitled to the benefits of screening.

Individually-Requested Screening: Epidemiological Characteristics, Ethical Foundations, Evidence Requirements

We define “individually requested” screening tests as those which have not been recommended at the population level, but which are nonetheless sought by patients or offered by physicians on an ad-hoc basis when either party is concerned about latent disease and believes that early detection may provide life-saving benefits. Individually requested screening tests lack high-level evidence of population benefit from RCTs, and most CT screening tests fit into this category. Examples include lung screening CT in smokers, brain CT angiography (CTA) or magnetic resonance angiography (MRA) screening for cerebral aneurysms, and whole-body screening CT.

The state of evidence for individually requested screening tests varies greatly, from screening examinations with no trial data (as for whole-body screening CT) to examinations for which trials have established that screening detects disease earlier in its course but have not yet concluded that screening improves population outcomes (as for lung CT screening in smokers) (Black et al. 2006; Henschke et al. 2006). Most CT screening examinations are not considered by professional societies, governmental bodies, or insurers to have sufficient levels of evidence of population benefit to recommend population screening. In some cases, such as for cerebral aneurysm screening, professional societies are largely silent and strong guidelines do not exist. In other cases, such as for whole-body CT screening, professional societies actively discourage screening. In the case of lung cancer screening, professional guidelines state that current evidence is insufficient to recommend for or against routine lung cancer CT screening in people older 60 years who have smoked for more than 20 years (US PSTF 2006; Strauss et al. 2005).

²It should be noted that groups such as the US PSTF does not always require RCT-type evidence before recommending a screening test: Pap smears, for example, are supported by evidence from multiple observational studies (Woolf et al. 1996).

Despite the lack of endorsement, CT screening tests are readily available for use and direct-to-consumer marketing efforts have encouraged patients to seek screening. Under such circumstances, individual physicians and patients need to consider whether screening is appropriate. This leads to a more fundamental question about how to incorporate existing evidence—specifically, evidence at a level lower than RCT-type evidence—into individual patient care decisions. While the “evidence” of evidence-based medicine is often defined in terms of outcomes-based research on *populations*, applying EBM to *individual* cases is a complex problem. Sackett and colleagues (1996) has stated that:

EBM is the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients, taking into account individual patients’ predicaments, rights, and preferences using best evidence from clinically relevant research (71).

Using this concept of EBM, Ashby and colleagues have argued that Bayesian decision-making is a useful model for incorporating evidence from clinical trials into individual patient care decisions (Ashby and Smith 2000). Bayesian models consider the best available evidence based upon population studies, as well as individual patient risk factors, characteristics, values, and the clinician’s insights. This approach can be helpful for individual decision-making in light of uncertain or inconclusive evidence. Bayesian belief networks are already being developed to aid in the interpretation and management decisions for patients undergoing mammography (Burnside et al. 2000, 2006). Further, Bayesian decision-making may be particularly useful for individual screening decisions when practice guidelines conclude that there is insufficient evidence to either support or oppose a screening test for a population.

The differences between population-based screening and individually requested screening imply, in our view, that the two types of decision-making may require different levels of evidence. Promoting the good of the population is the main objective of public health policy decisions, which affect large numbers of people and require substantial investment of public resources. Decisions to recommend screening for a population, therefore, should be based upon the highest possible level of evidence of population benefit from clinical trials. Promoting the good of the individual patient is the main objective of individual patient care decisions. Decisions to recommend screening for an individual, therefore, should be based upon an individual’s risk profile and preferences in addition to the best available evidence. These individually based decisions, we believe, may not require the higher levels of evidence, such as RCTs, that are desirable for population-based decisions. Rather, individual patient and physician characteristics and values may be given more weight in the decision-making process regarding individually requested screening.

The next section focuses on how physicians ought to respond to patient requests for screening examinations when the population risks and benefits are still uncertain. We examine various combinations of scientific evidence, professional guidelines, patient risk factors and preferences, and physician beliefs in order to more precisely demarcate when an individually requested screening examination is and is not appropriate. Indeed, we suggest that it may be appropriate in certain cases to allow patients access to screening even before RCT-level evidence and professional guidelines support population screening. We include a description of the particular safeguards we feel should be in place when individually requested screening is considered.

ROLES AND RESPONSIBILITIES OF PHYSICIANS REGARDING INDIVIDUALLY REQUESTED SCREENING

Given that many new screening examinations lack the level of evidence to be recommended as population-based screening tools, how should individual physicians respond when their patients express interest in obtaining such examinations? There may be a great deal of pressure from worried patients, industry, medical–legal concerns about missing latent disease, and the technological imperative in medicine to provide new tests, particularly image-based screening tests that visualize the anatomy in spectacular detail.

All physicians who consider adopting new screening technology, in our view, have a minimum set of basic responsibilities to protect the welfare of their patients. First, physicians ought to understand the epidemiological basis for evaluating and recommending screening tests for populations. This includes understanding the pitfalls of length time, lead time, and overdiagnosis biases that compromise the validity of certain study designs, as well as understanding the potential for false-positive and false-negative results and the risks, costs, and psychological stress for patients associated with follow-up tests and procedures. Second, physicians should evaluate the existing literature and consult professional society guidelines regarding screening tests that their patients may request. Such awareness of the state of evidence and professional recommendations is essential in order for physicians to better evaluate whether screening may be in their patients' best interests. This will also help them explain to patients the potential risks, benefits, and uncertainties of the screening examination.

The third basic responsibility for physicians is to advocate or, when possible, be involved in early, formal evaluation of new screening tests for which there is a poor evidence base. We believe that all physicians have a professional duty to incorporate evidence into their decision-making and the field should encourage research to formally evaluate innovative practices. While it is unlikely to be financially or practically feasible to conduct an RCT for each screening test that emerges in practice, other study designs and forms of evidence—well-controlled observational studies and computer-based decision analysis (Gazelle et al. 2005), for example—are more easily produced and may inform screening practices. When feasible, physicians should consider becoming involved in such studies that, when begun early in the application of a new screening test, can gather valuable information about the sensitivity and specificity of the test and provide the initial “proof of concept” that screening can at least detect disease early in its progression (Woolf et al. 1996).

The fourth basic responsibility for physicians is to refrain from engaging in direct-to-consumer advertising of screening services to patients before they are recommended for the population. Research suggests that people often overestimate the benefits and underestimate the risks from various cancer screening tests (Katapodi et al. 2004; Marcus 1999; Schwartz et al. 2004; Vernon 1999; Woloshin et al. 2000). Further, research on direct-to-consumer advertising of pharmaceuticals suggests that many consumers assume that all advertised drugs are safe and/or effective (Bell et al. 1999). It is possible that consumers may falsely infer that any screening examination advertised by physicians offers more benefits than risks and/or is recommended by physicians as a whole. Given the high likelihood of misleading patients, consumer advertising before screening is endorsed for a population, in our view, is unprofessional.

After fulfilling these basic responsibilities, individual physicians will still need to decide whether a new screening test is appropriate for specific patients in their care. Making the decision to screen a patient in light of inconclusive evidence of population benefit is difficult and involves weighing several different factors. We suggest physicians and patients consider

four primary factors, based on the Bayesian approach described earlier, to address these decisions: 1) the strength of evidence and nature of professional recommendations for a particular screening examination, 2) the patient's risk factors for the screened disease, 3) the patient's valuation of screening information, and 4) the clinician's own experience and intuitions. The following paragraphs explore three specific scenarios with variable evidence-based professional recommendations, using the US PSTF language and levels of evidence as a guide when possible. The US PSTF grades the strength of its evidence-based recommendations from "A" (*strongly recommends*), "B" (*recommends*), "C" (*no recommendation for or against*), "D" (*recommends against*), or "I" (*insufficient evidence to recommend for or against*) (Harris et al. 2001). We focus on screening tests with D- and I-type level recommendations, as these are the categories under which most CT screening examinations currently fall, examining how patient characteristics and values and physician preferences ought to weigh and balance at each of these levels. Importantly, we acknowledge that screening decisions will be highly context-dependent, as the nature of disease, risks inherent to the screening test, and invasiveness and costs of follow-up studies will vary greatly among screening tests. Nevertheless, we outline the important considerations for several common CT screening scenarios that physicians and patients may face.

Case 1: Professional Society Guidelines Discourage the Screening Examination. ("Class D"-Type Recommendations)

The first case we consider involves a screening examination that is explicitly discouraged by professional society guidelines, or has a "class D"-type level recommendation. Such screening examinations may have either no or low-quality evidence of benefit for populations or may have sufficiently strong evidence of patient harm. Low-quality evidence includes evidence from uncontrolled case series or poorly controlled observational studies. An example of such a situation would be a whole-body CT scan requested by an asymptomatic, healthy 55-year-old individual with no risk factors except age, who wants to gain peace of mind. There have been no clinical trials to evaluate the benefit of whole-body CT screening, and many professional societies explicitly discourage this examination (US Food and Administration [US FDA] 2002; American Medical Association [AMA] Council on Scientific Affairs 2003; US PSTF 2004a; ACR 2004).

Physicians should generally discourage individual patients from screening when there is no or poor evidence and professional society discouragement, regardless of their personal beliefs about the utility of the examination, the patients' risk profile, and patient beliefs and preferences for screening. There are several reasons for this position. First, in this case, the potential risks and benefits of screening are poorly understood, making it quite difficult for a physician to estimate whether the test will be on balance beneficial. Discouraging screening in such cases coheres with a physician's professional duties to protect patients from tests that may cause more harms than benefits, including diagnostic screening tests of great uncertainty. Further, we agree with Doukas and colleagues (1997) that, by educating their patients about the risks and benefits of the screening test, physicians may "articulate the boundaries of their own professional integrity, for patients cannot compel physicians to render services that run counter to their best professional and ethical judgment" (486).

A secondary concern in this case has to do with the judicious use of shared healthcare resources. It has been argued that a just health system should not tolerate the proliferation of expensive, unproven therapies that lead to spiraling costs and shift resources away from more urgent healthcare needs, even if the market would support this (Sox 2001). As care provided to one patient will most likely affect the care available to others, denying patient requests for screening in this case coheres with a physician's duty to act as a prudent

steward of shared healthcare resources by discouraging costly tests with poorly understood likelihood of medical benefit.

Some have argued that as long as informed consent explains the risks, benefits, and uncertainties, patients should be able to access screening services that they believe will benefit them, particularly if they are willing to assume the costs (Amis 2003; Brant-Zawadzki 2002a, 2002b). We disagree with this view, however, particularly for screening tests of class D-type level recommendation. While physicians should generally take into account patient preferences in medical decision-making, screening decisions are particularly complex and challenging. Previous research on screening with mammography, prostate-specific antigen (PSA), and colonoscopy suggests that patients generally tend to overestimate the benefits and underestimate the risks of screening tests (Schwartz et al. 2000, 2004; Silverman et al. 2001; Volk et al. 1999, 2003; Woloshin et al. 2000). Importantly, the recent increase of direct-to-consumer marketing of screening puts patients at risk of making harmful choices in the absence of adequate guidance and constraints. That is, the context has changed such that some information coming from health professionals (i.e. screening advertisements) is not based on a clear, balanced presentation of existing evidence.

Even if the individual requesting the whole-body CT had a good understanding of the uncertainties of the test and believed he would derive great psychological benefit from screening, these potential psychological benefits are inadequate, in our view, to outweigh the potential medical risks, including radiation exposure, false-positive results leading to invasive, risky, and costly follow-up procedures, false negatives, and the detection of pseudo-disease. The primary goal of medicine, including the administration of medical services, is to benefit patients' health (Beauchamp and Childress 2000; Pellegrino 2001). As such, patients should not have free access to any medical test or treatment they desire and can pay for, as they would for other types of goods and services. Indeed, constraining patient autonomy under the conditions of Case 1 is appropriate, in our view, as physicians should actively protect them from medical products of poorly quantified risks and benefits.

A variation on this case includes a situation in which a physician actually believes the benefits of screening could outweigh the harms for a particular patient, despite no or low quality evidence of its benefit and professional societies discouragement. A physician may encounter particular patients with strong risk factors for disease who place great value on the knowledge derived from screening. One example could be a patient with a family history of pancreatic cancer who would like a whole-body CT screen to rule out this aggressive cancer for reassurance. The US PSTF (2004b) recommendations explicitly discourage whole-body CT screening for this purpose. Initial, small prospective studies suggest that screening patients with a strong family history can detect disease early, while the impact of screening on long-term mortality remains unknown (Canto et al. 2006). While cases like these are difficult, we commend a conservative approach that gives more weight to the low level of evidence and to professional society guidelines than to individual patient and physician preferences; clinicians should generally not provide screening examinations that have low level or no evidence and are discouraged by professional societies.

Case 2: Professional Society Guidelines are Neutral or Non-Existent

The second case we consider involves a screening examination for which professional recommendations are either neutral or non-existent. The evidence for such screening examinations may be of low quality, sparse, or in the early stages of production. One current example of this situation could include using magnetic resonance imaging (MRI) and/or MRA of the brain to screen for cerebral aneurysms in patients with a positive family history. The US PSTF does not have specific guidelines for cerebral aneurysm screening. The only

official guideline comes from the Stroke Council of the American Heart Association (Dallas, TX), stating that while current evidence argues neither for nor against population screening, clinicians may consider it for particular patients on an individual basis. (Bederson et al. 2000). Currently, few studies have evaluated the use of MRI/MRA as screening tests, and there is no evidence that cerebral aneurysm screening benefits population morbidity or mortality (Crawley et al. 1999; The Magnetic Resonance Angiography in Relatives of Patients with Subarachnoid Hemorrhage Study Group 1999). Scenarios such as these are common, and the lack of directive guidelines implies that physicians and patients need to draw upon factors other than evidence to make decisions about screening (Woolf et al. 1996).

Similar to Case 1, physicians and patients should be aware that screening under these circumstances may expose patients to poorly quantified risks and benefits. And, although neutral professional society guidelines may appear an invitation for physicians to engage in screening as they like, there is another reason to be cautious about granting patients access to screening tests that have a poor evidence base: this may slow the progression of research that aims to better characterize the risks and benefits of the test. If physicians were to commonly grant patient requests for unproven screening test when there is no or low quality evidence and neutral guidelines, the motivation to conduct or participate in research trials to formally evaluate the test may diminish. Indeed, granting patients access to such screening tests may lead to their gradual diffusion into practice, potentially becoming understood as standard of care and further delaying our ability to characterize the risks and benefits of a screening examination. As mentioned previously, there are numerous examples of medical treatments that have diffused into practice in such a manner, only later to be proven ineffective or harmful to patients after more formal evaluation. These include internal mammary artery ligation for angina (Cobb et al. 1959; Dimond et al. 1960), internal carotid artery bypass to prevent the recurrence of stroke (Group 1985), and bone marrow transplantation for breast cancer (Mello and Brennan 2001). The delay in rigorous evaluation of these treatments caused thousands of patients to suffer harms from unnecessary and non-beneficial interventions. Thus, commonly allowing patients access to a screening test at a stage when there is no or low-quality evidence of benefit poses a threat to the research enterprise and, ultimately, to patient welfare.

The best approach, in our view, would be for physicians to discourage screening in most cases with neutral or non-existent recommendations and advocate better evaluation of screening. For patients with well-defined risk factors who would greatly value information from a particular screening examination, such as a patient with cardiovascular risk factors and first-degree relatives who have died from cerebral aneurysm rupture, physicians should consider encouraging enrollment in research trials that will bolster the evidence base for a screening test. This may constrain both patient and physician autonomy. However, in general these constraints are justified for all of the reasons given in Case 1: protecting patients from poorly quantified harms, protecting them from possible overestimated expectation of benefits, and curbing waste in the healthcare system. An additional justification is the desire to move research forward in an expedient manner so that the results can benefit individual and population-level decision-making as soon as possible, particularly when professional society guidelines are non-directive.

Case 3: Professional Society Guidelines State Evidence is Insufficient to Recommend For or Against a Screening Test ("Class I" Recommendation)

The last case we consider involves a screening examination with class I-type level recommendations. According to the US PSTF, class-I recommendations state that evidence is insufficient to recommend for or against routine population screening because evidence that the screening test is effective does not exist, is of low quality, or conflicting (US PSTF

2007b). We wish to focus on situations in which the screening test has undergone substantial evaluation and there is valid evidence from properly controlled observational studies suggesting that a screening test detects disease at earlier stages, but data from RCTs has not yet emerged to establish the benefit (or “effectiveness”) for population outcomes. These cases, in our view, may be the most complex and controversial. Lung CT screening in smokers is a current example of this situation (USPSTF 2004c). There is great debate in the medical literature about whether it is appropriate to offer smokers chest CT screening, either on an individual basis or at the population level. Smoking is a well-established risk factor for lung cancer, (Samet 1993) and controlled observational trials have established that lung CT in smokers detects lung cancer at earlier stages. Several RCTs are currently underway to determine whether screening smokers will decrease lung-cancer related mortality (Gohagan et al. 2004; NLST 2007; Swensen et al. 2005; Xu et al. 2006). Those in favor of screening worry that patients are being deprived of a life-extending test while we wait for RCT-level data to arrive (Henschke et al. 2006). Others counter that there is no guarantee that early detection will lead to a reduction in population-based mortality, and the relatively great risks and costs associated with the follow-up of asymptomatic lung lesions must be balanced against higher-level proof of population benefit (Patz et al. 2001; Swensen et al. 2005).

Under such circumstances, in light of a class I-type level recommendation, we argue that it may be appropriate for physicians and patients who greatly value potential information from screening to engage in screening provided certain conditions are met. First, the patient should have well-defined risk factors for the disease to be screened. Importantly, these risk factors should be specified by either a group of clinical experts or clinical research collaborators as helpful in defining which patients are likely to benefit from screening. For example, the NLST has used pack-year smoking history and age to demarcate the high-risk population that may benefit from lung cancer screening with chest CT. In order to minimize the risks and maximize the potential benefits from individually based screening, therefore, defined risk factors for the screened disease should exist in order to place a patient within or outside of the potential target population. The second condition for screening under class I-type recommendations is that well-controlled observational trial data should have already established that a screening test increases early detection rates in the target population and that RCTs are well underway. Lung cancer screening with chest CT could meet these two conditions for certain patients.

Under these two conditions, it is reasonable to believe that the benefits of screening could outweigh the harms for an individual patient, even when clinical trials have not yet established a mortality benefit at the population level. While offering screening in this scenario may expose patients to the risks and unknowns of screening and compromise the expediency of research, these drawbacks may be attenuated in certain circumstances; specifically, if previous research and preliminary data from ongoing clinical trials point strongly toward a potential benefit and have well characterized aspects such as sensitivity and specificity of screening, concerns about exposing patients to the harms of screening without any benefit are reduced. Further, for screening tests in which RCTs are ongoing, there is less of a concern that offering patients screening outside of trials jeopardizes the research enterprise. Thus, the threats to patient welfare and research expediency in Case 3 may be at a level low enough to allow for patient and physician preferences to weigh more heavily in the decision of whether or not to screen.

As Malm (1999) has argued, while it is important to ground population-based screening recommendations in the best possible evidence rather than upon assumptions about the value of early detection, “a screening recommendation is ethically justified only if the test reasonably can be expected to be beneficial on balance to the person taking it” (33). Under the two conditions described previously, we believe that individual physicians and patients

may have adequate information to expect a screening test to be beneficial on balance. Indeed, denying all individual requests for any screening examination until the completion of RCTs is too rigid, absolute, and unrealistic a position for several reasons. First, performing RCTs for every potential screening test will never be practically feasible; the quality of evidence exists on a continuous spectrum, and thinking intelligently about where we are on that spectrum is more important than designating absolute “cutoffs” of evidence below which any screening is unacceptable. Second, it is important to allow some space for individual patient desires and physician judgment to enter the decision-making process under conditions of uncertainty. As we have noted, one option might be to encourage physicians who screen patients before RCT-level evidence is available to contribute their patients’ information to a national database that would collect observational data on screening.

We consider briefly the analogy between early access to new screening tests and early access to new pharmaceuticals for severely ill patients who have exhausted standard treatment options. The conflict between conducting thorough research and accommodating individual patient access to promising, potentially life-saving therapies gained unprecedented attention in the midst of the AIDS epidemic in the late 1980s. Severely ill patients who could not gain entry to clinical trials fought for access to those unproven therapies off-label, arguing the risk-benefit analysis made sense given that they were facing certain death. This debate has evolved to the point where many pharmaceutical companies and the US FDA have provisions for granting patients with a variety of severe diseases off-label access (“compassionate use”) to investigational new drugs, provided early phase clinical trials have shown promise and certain safeguards are in place to track patient outcomes. (Pfizer 2008; Thompson 2000). Important lessons for screening can be drawn from the history of off-label pharmaceutical use. Yet, while similar ethical tensions arise in both settings—respecting patient autonomy, protecting against unknown risks, promoting population benefits via research—important differences between the nature of screening and treating life-threatening illness may imply a different threshold for access. Certainly, novel pharmaceuticals pose more immediate and potentially more severe harms than do diagnostic screening tests. Likewise, such interventions potentially offer more immediate benefits for severely ill patients than do screening tests for apparently healthy ones. In our view, the more urgent situation of patients without standard treatment options provides a more compelling reason to provide early access, assuming there is adequate surveillance and treatment of adverse events and outcomes, and that clinical trials are already adequately populated to produce population-level evidence.

While it may be appropriate for individual physicians to refer eager patients with defined, specific risk factors for screening in certain cases, it is important that safeguards and quality assurance mechanisms are in place to maximize the benefit of screening under these conditions. The appropriateness of screening also depends upon, we argue, the quality of the informed consent process, quality of screening equipment, and thoroughness of follow-up of screening results with patients and their physicians. Because all of these factors are provided in the controlled setting of a research trial, the option to offer eligible patients trial enrolment is even more attractive. The following paragraphs articulate why these particular features can make screening individual patients appropriate, despite lack of conclusive evidence about population benefit.

Criteria and Safeguards for Granting Patient Access to Unproven Screening Examinations, Outside the Research Context

A critical safeguard for screening patients with an unproven examination is a thorough informed consent process to ensure patients understand the potential risks, benefits, and uncertainties of the screening test. This is particularly crucial given ample evidence to

suggest that people often misperceive the goals or effects of cancer screening, are poor estimators of their personal cancer risk, and are generally enthusiastic about cancer screening (Katapodi et al. 2004; Kreuter 1999; Marcus 1999; Schwartz et al. 2004; Vernon 1999; Woloshin et al. 2000). For example, in a study of the general population's attitudes toward cancer screening, Schwartz and colleagues (2004) found that patients had a strong enthusiasm for cancer screening, both for specific cancers and whole-body screening, even despite past personal experience with false positives and unnecessary work-up. When asked about whole-body CT screening, 86% of respondents wanted a free scan. Of these, 73% would rather have a scan than \$1000 and only 27% mentioned there may be a downside to a body CT scan: 14% mentioned false-positive results and 3% unnecessary work-up (Schwartz et al. 2004). Other studies reveal that people are quite tolerant of false positive screening results, have a poor understanding of pseudo-disease, overestimate the benefits from screening, and perceive screening as a primary rather than secondary prevention tool. (Aiken et al. 1995; Domenighetti et al. 2003; Schwartz et al. 2000). As Schwartz and colleagues (2004) have noted, public misperceptions about the benefits and burdens from screening, combined with a "cultural enthusiasm for screening create an environment ripe for the premature diffusion of screening technologies, placing the public at risk of overtesting and overtreatment" (71).

Given evidence that people often misestimate the risks and benefits from both proven and unproven screening examinations, the appropriateness of screening will hinge heavily upon the quality of the informed consent process. For some patients, such a process may dissuade them from screening despite their initial eagerness. For example several studies indicate that men are less likely to be interested in screening for prostate cancer with PSA testing if they are made aware of the 'pros,' 'cons,' and uncertainties during informed consent. (Flood et al. 1996; Volk et al. 1999; 2003; Wolf et al. 1996). The population benefit of routine PSA screening in men older than age 50 years has not been established, and professional society guidelines do not currently recommend routine screening (US PSTF 2002). Many have advocated that risk communication for PSA screening should aim at more neutral informed consent or shared decision-making to help ensure that patients make screening decisions that are in their best interests (Chan and Sulmasy 1998; Chan et al. 2003; Vernon 1999). After patients have an adequate understanding of the risks, benefits, and uncertainties of the screening examination, they can better decide whether such risks and unknowns are acceptable to them.

While we agree that physicians should strive to provide information about risks, benefits, and uncertainties, there will remain disputes in the field about what sort and how much information to provide patients. For example, research suggests that physicians have different notions of what patients should be told about PSA screening during informed consent. A study by Chan and colleagues (2003) revealed that, despite professional guidelines supporting informed decision making, non-urologists were more likely than urologists to rate facts reflecting uncertainty as highly important for men to know, including statements about prostate cancer risk, screening with PSA, and treatment. Individual physicians could be better guided in their approach to consent by more explicit guidelines from professional societies regarding the specific types of risks, benefits, and uncertainties that should be stressed to patients. One interesting model is provided by a recent outline of information for patients about the risks, benefits, uncertainties, and state of evidence associated with lung cancer CT screening. (Strauss et al. 2005).

Another safeguard for screening patients before population screening is recommended involves using screening equipment of adequate quality. Some have expressed concern that the use of older scanners, lack of intravenous contrast, or lack of adequate radiologist training in a particular modality or organ system compromises the sensitivity and specificity

of screening examinations, producing results that are difficult to interpret and may lead to more diagnostic testing (Berlin 2003; Fishman and Horton 2002). For screening tests that have already been validated and considered standard of care, it is likely that guidelines will already exist regarding equipment quality, technical standards, and required physician training. Radiologists reading mammograms, for example, must be certified and are required to read a minimum number of studies per year. Such technical and training guidelines will not exist for screening tests of unproven value, opening the door to variations in techniques and competency potentially harmful to test validation and patient well being. One example of this situation is provided by MRA for cerebral aneurysm detection, where there is preliminary evidence to suggest that the detection rate depends upon the quality of the equipment and the training of the radiologist in three-dimensional imaging of the cerebral vasculature (Schwab et al. 2008).

The final safeguard to providing appropriate screening is to establish routine mechanisms to ensure timely communication of the results to the primary care physician, adequate counseling of patients about the meaning of results, and timely follow-up of any positive findings. Patients should be referred for screening from their primary care physician, who has discussed their understanding of and expectations for screening. The physician's referral, combined with thorough follow-up of results, is particularly important in light of recent data from Illes and colleagues indicating great variability in the manner and extent to which results of self-referred CT screening examinations were communicated with physicians and patients (Illes et al. 2003).

CONCLUSION

Engaging in individual-based screening before population-based screening is endorsed by evidence and professional guidelines raises timeless questions about physicians' duties in the setting of innovation and the scope of patient autonomy to access new technology. We hope that the issues and cases presented here may help guide individual physicians as they consider how to respond to patient requests for new screening examinations.

To best balance the goals of consumer protection, patient autonomy, and prudent innovation, we believe it generally inappropriate for physicians and patients to engage in individually requested screening. There may be a few exceptions, however: when rigorously-designed clinical trials are underway and good evidence already exists to suggest potential population benefit from screening, when well-defined, specific patient risk factors for disease have been articulated, and when patients and clinicians both value screening information. Such screening activities should employ specific safeguards, including careful informed consent, high-quality equipment, and thorough follow-up of results. Despite these individual exceptions, referring physicians and the field as a whole should be vigilant in the appraisal of evidence, and continue to support formal evaluation of new screening examinations. This will better ensure that the best evidence is available for patients and their physicians to make good choices about screening.

REFERENCES

- Aiken LS, Fenaughty AM, West SG, Johnson JJ, Luckett TL. Perceived determinants of risk for breast cancer and the relations among objective risk, perceived risk, and screening behavior over time. *Women's Health*. 1995; 1:27–50.
- American College of Radiology (ACR). Position Statement on Full-Body CT Screening. 2004. Available at: www.acr.org
- American Medical Association (AMA) Council on Scientific Affairs. Featured Report: Commercialized Medical Screening (A-03). American Medical Association. 2003. Available at: <http://www.ama-assn.org/ama/no-index/about-ama/13628.shtml>

- Amis ES Jr. CT screening. *Radiology*. 2003; 228:901–902. [PubMed: 12954905]
- Ashby D, Smith AF. Evidence-based medicine as Bayesian decision-making. *Statistics in Medicine*. 2000; 19:3291–3305. [PubMed: 11113960]
- Ashcroft RE. Current epistemological problems in evidence based medicine. *Journal of Medical Ethics*. 2004; 30:131–135. [PubMed: 15082804]
- Beauchamp, T.; Childress, J. *Principles of Biomedical Ethics*. 5th ed.. New York, NY: Oxford University Press; 2000.
- Bederson JB, Awad IA, Wiebers DO, et al. Recommendations for the management of patients with unruptured intracranial aneurysms: A Statement for healthcare professionals from the Stroke Council of the American Heart Association. *Stroke*. 2000; 31:2742–2750. [PubMed: 11062304]
- Bell RA, Kravitz RL, Wilkes MS. Direct-to-consumer prescription drug advertising and the public. *Journal of General Internal Medicine*. 1999; 14:651–657. [PubMed: 10571712]
- Berlin L. Should whole-body CT screening be performed with contrast media? *American Journal of Roentgenology*. 2003; 180:323–325. [PubMed: 12540424]
- Black C, Bagust A, Boland A, et al. The clinical effectiveness and cost-effectiveness of computed tomography screening for lung cancer: Systematic reviews. *Health Technology Assessment*. 2006; 10(iii–iv, ix–x):1–90.
- Black WC, Welch HG. Advances in diagnostic imaging and overestimations of disease prevalence and the benefits of therapy. *New England Journal of Medicine*. 1993; 328:1237–1243. [PubMed: 8464435]
- Black WC, Welch HG. Screening for disease. *American Journal of Roentgenology*. 1997; 168:3–11. [PubMed: 8976910]
- Brant-Zawadzki M. CT screening: Why I do it. *American Journal of Roentgenology*. 2002a; 179:319–326. [PubMed: 12130426]
- Brant-Zawadzki MN. Screening on demand: Potent of a revolution in medicine. *Diagnostic Imaging*. 2000; 22:25–27. [PubMed: 11146799]
- Brant-Zawadzki MN. Screening CT: Rationale. *Radiographics*. 2002b; 22:1532–1536. discussion 6–9. [PubMed: 12432125]
- Burnside E, Rubin D, Shachter R. A Bayesian network formammography. *AMIA Annual Symposium Proceedings*. 2000:106–110.
- Burnside ES, Rubin DL, Fine JP, Shachter RD, Sisney GA, Leung WK. Bayesian network to predict breast cancer risk of mammographic microcalcifications and reduce number of benign biopsy results: Initial experience. *Radiology*. 2006; 240:666–673. [PubMed: 16926323]
- Canto MI, Goggins M, Hruban RH, et al. Screening for early pancreatic neoplasia in high-risk individuals: A prospective controlled study. *Clinical Gastroenterology and Hepatology*. 2006; 4:766–781. quiz 665. [PubMed: 16682259]
- Chan EC, Sulmasy DP. What should men know about prostate-specific antigen screening before giving informed consent? *American Journal of Medicine*. 1998; 105:266–274. [PubMed: 9809686]
- Chan EC, Vernon SW, Haynes MC, O'Donnell FT, Ahn C. Physician perspectives on the importance of facts men ought to know about prostate-specific antigen testing. *Journal of General Internal Medicine*. 2003; 18:350–356. [PubMed: 12795733]
- Cobb L, Thomas G, Dillard D. An evaluation of internal-mammary-artery ligation by a double-blind technique. *New England Journal of Medicine*. 1959; 260:1115–1118. [PubMed: 13657350]
- Cochrane.org. Cochrane Collaboration. Available at: www.cochrane.org
- Cole P, Morrison AS. Basic issues in population screening for cancer. *Journal of the National Cancer Institute*. 1980; 64:1263–1272. [PubMed: 6767876]
- Crawley F, Clifton A, Brown MM. Should we screen for familial intracranial aneurysm? *Stroke*. 1999; 30:312–316. [PubMed: 9933265]
- Dimond EG, Kittle F, Crockett J. Comparison of internal mammary artery ligation and sham operations for angina pectoris. *American Journal of Cardiology*. 1960; 5:483–486. [PubMed: 13816818]

- Domenighetti G, D'Avanzo B, Egger M, et al. Women's perception of the benefits of mammography screening: Population-based survey in four countries. *International Journal of Epidemiology*. 2003; 32:816–821. [PubMed: 14559757]
- Doukas DJ, Fetter M, Ruffin MT, McCullough LB. Ethical considerations in the provision of controversial screening tests. *Archives of Family Medicine*. 1997; 6:486–490. [PubMed: 9305694]
- Fishman EK, Horton KM. Screening strategy joins contrast, noncontrast scans. *Diagnostic Imaging*. 2002; 24:45–47.
- Flood AB, Wennberg JE, Nease RF Jr, Fowler FJ Jr, Ding J, Hynes LM. The importance of patient preference in the decision to screen for prostate cancer. Prostate Patient Outcomes Research Team. *Journal of General Internal Medicine*. 1996; 11:342–349. [PubMed: 8803740]
- Franco EL, Morrison AS, Rohan TE. Evidence-based policy recommendations on cancer screening and prevention. *Cancer Detection and Prevention Journal*. 2002; 26:350–361.
- Gazelle GS, McMahon PM, Siebert U, Beinfeld MT. Cost-effectiveness analysis in the assessment of diagnostic imaging technologies. *Radiology*. 2005; 235:361–370. [PubMed: 15858079]
- Gohagan J, Marcus P, Fagerstrom R, Pinsky P, Kramer B, Prorok P. Baseline findings of a randomized feasibility trial of lung cancer screening with spiral CT scan vs chest radiograph: The Lung Screening Study of the National Cancer Institute. *Chest*. 2004; 126:114–121. [PubMed: 15249451]
- Group TEIBS. Failure of extracranial-intracranial arterial bypass to reduce the risk of ischemic stroke: Results of an international randomized trial. *New England Journal of Medicine*. 1985; 313:1191–1200. [PubMed: 2865674]
- Harris RP, Helfand M, Woolf SH, et al. Current methods of the US Preventive Services Task Force: A review of the process. *American Journal of Preventive Medicine*. 2001; 20:21–35. [PubMed: 11306229]
- Henschke CI, Yankelevitz DF, Libby DM, Pasmantier MW, Smith JP, Miettinen OS. Survival of patients with stage I lung cancer detected on CT screening. *New England Journal of Medicine*. 2006; 355:1763–1771. [PubMed: 17065637]
- Hillman BJ. CT screening: Who benefits and who pays. *Radiology*. 2003a; 228:26–28. [PubMed: 12832572]
- Hillman BJ. Economic, legal, and ethical rationales for the ACRIN national lung screening trial of CT screening for lung cancer. *Academic Radiology*. 2003b; 10:349–350. [PubMed: 12643562]
- Illes J, Fan E, Koenig BA, Raffin TA, Kann D, Atlas SW. Self-referred whole-body CT imaging: Current implications for health care consumers. *Radiology*. 2003; 228:346–351. [PubMed: 12893896]
- Illes J, Kann D, Karetzky K, et al. Advertising, patient decision making, and self-referral for computed tomographic and magnetic resonance imaging. *Archives of Internal Medicine*. 2004; 164:2415–2419. [PubMed: 15596630]
- Kalish GM, Bhargavan M, Sunshine JH, Forman HP. Self-referred whole-body imaging: Where are we now? *Radiology*. 2004; 233:353–358. [PubMed: 15459320]
- Katapodi MC, Lee KA, Facione NC, Dodd MJ. Predictors of perceived breast cancer risk and the relation between perceived risk and breast cancer screening: a meta-analytic review. *Preventive Medicine*. 2004; 38:388–402. [PubMed: 15020172]
- Kopans DB, Monsees B, Feig SA. Screening for cancer: When is it valid? Lessons from the mammography experience. *Radiology*. 2003; 229:319–327. [PubMed: 14595137]
- Kreuter MW. Dealing with competing and conflicting risks in cancer communication. *Journal of the National Cancer Institute—Monographs*. 1999; 25:27–35. [PubMed: 10854454]
- Lee TH, Brennan TA. Direct-to-consumer marketing of high-technology screening tests. *New England Journal of Medicine*. 2002; 346:529–531. [PubMed: 11844859]
- The Magnetic Resonance Angiography in Relatives of Patients with Subarachnoid Hemorrhage Study Group. Risks and benefits of screening for intracranial aneurysms in first-degree relatives of patients with sporadic subarachnoid hemorrhage. *New England Journal of Medicine*. 1999; 341:1344–1350. [PubMed: 10536126]
- Malm HM. Medical screening and the value of early detection. When unwarranted faith leads to unethical recommendations. *Hastings Center Report*. 1999; 29:26–37. [PubMed: 10052009]

- Marcus AC. New directions for risk communication research: a discussion with additional suggestions. *Journal of the National Cancer Institute—Monographs*. 1999; 25:35–42. [PubMed: 10854455]
- Meakins JL. Innovation in surgery: The rules of evidence. *American Journal of Surgery*. 2002; 183:399–405. [PubMed: 11975927]
- Mello MM, Brennan TA. The controversy over high-dose chemotherapy with autologous bone marrow transplant for breast cancer. *Health Affairs*. 2001; 20:101–117. [PubMed: 11558695]
- Morrison, A. *Screening in Chronic Disease*. New York, NY: Oxford University Press; 1992. p. 3-20.
- National Cancer Institute. National Lung Screening Trial. 2005. Available at: <http://www.cancer.gov/NLST>
- Obuchowski NA, Graham RJ, Baker ME, Powell KA. Ten criteria for effective screening: Their application to multislice CT screening for pulmonary and colorectal cancers. *AJR American Journal of Roentgenology*. 2001; 176:1357–1362. [PubMed: 11373191]
- Patz EF Jr, Black WC, Goodman PC. CT screening for lung cancer: not ready for routine practice. *Radiology*. 2001; 221:587–591. 598–599. [PubMed: 11719648]
- Pellegrino ED. The internal morality of clinical medicine: a paradigm for the ethics of the helping and healing professions. *Journal of Medicine and Philosophy*. 2001; 26:559–579. [PubMed: 11735050]
- Pfizer, RaD. Policy on compassionate use. 2008. Available at http://www.pfizer.com/research/science_policy/compassionate_use_policy.jsp
- Pocock, S. *Clinical Trials—A Practical Approach*. Chichester, UK: Wiley; 1983.
- Sackett DL, Rosenberg WM, Gray JA, Haynes RB, Richardson WS. Evidence based medicine: what it is and what it isn't. *BMJ: British Medical Journal*. 1996; 312:71–72.
- Samet J. The epidemiology of lung cancer. *Chest*. 1993; 103:20S–29S. [PubMed: 8416770]
- Schwab KE, Gailloud P, Wyse G, Tamargo RJ. Limitations of magnetic resonance imaging and magnetic resonance angiography in the diagnosis of intracranial aneurysms. *Neurosurgery*. 2008; 63:29–34. [PubMed: 18728566]
- Schwartz LM, Woloshin S, Fowler FJ Jr, Welch HG. Enthusiasm for cancer screening in the United States. *JAMA*. 2004; 291:71–78. [PubMed: 14709578]
- Schwartz LM, Woloshin S, Sox HC, Fischhoff B, Welch HG. US women's attitudes to false positive mammography results and detection of ductal carcinoma in situ: cross sectional survey. *BMJ: British Medical Journal*. 2000; 320:1635–1640.
- Siedt D. Insurance firms say body scans are 'retail medicine'. *Daily Record*. 2004 July 9. Available at www.mddailyrecord.com.
- Silverman E, Woloshin S, Schwartz LM, Byram SJ, Welch HG, Fischhoff B. Women's views on breast cancer risk and screening mammography: A qualitative interview study. *Medical Decision Making*. 2001; 21:231–240. [PubMed: 11386630]
- Sox H. *Annals of Internal Medicine's Harold Sox, MD, discusses physician charter of professionalism*. Interview by Brian Vastag. *JAMA*. 2001; 286:3065–3066. [PubMed: 11754654]
- Strauss, GM.; Dominioni, L.; Jett, JR.; Freedman, M.; Grannis, FW, Jr. Como international conference position statement: lung cancer screening for early diagnosis 5 years after the 1998 Varese conference; *Chest*; 2005. p. 1146-1151.
- Sunshine JH, Applegate KE. Technology assessment for radiologists. *Radiology*. 2004; 230:309–314. [PubMed: 14752174]
- Swensen SJ, Jett TE, Hartman SJ, et al. CT screening for lung cancer: Five-year prospective experience. *Radiology*. 2005; 235:259–265. [PubMed: 15695622]
- Thompson, L. Experimental treatment? Unapproved but not always unavailable. *FDA Consumer Magazine*. 2000. Available at http://www.fda.gov/fdac/features/2000/100_exp.html
- United States Food and Administration (USFDA). Whole Body Scanning Using Computed Tomography. 2002. Available at: <http://www.fda.gov/cdrh/ct/>
- United States Preventive Services Task Force (USPSTF). USPSTF. Cancer Screening Recommendations. 2004a. Available at: <http://www.ahrq.gov/clinic/uspstfix.htm>
- USPSTF. Screening for Pancreatic Cancer. 2004b. Available at: <http://www.ahrq.gov/clinic/uspstf/uspstpanc.htm>

- USPSTF. Screening for Lung Cancer. 2004c. Available at:
<http://www.ahrq.gov/clinic/uspstf/uspstlung.htm>
- USPSTF. Screening for Prostate Cancer: Recommendations and Rationale. 2006. Available at:
<http://www.ahrq.gov/clinic/3rduspstf/prostatescr.htm>
- USPSTF. Appendix A: How the U.S. Preventive Services Task Force Grades Its Recommendations. 2007a. Available at: <http://www.ahrq.gov/clinic/pocketgd/gcpsapp.htm>
- USPSTF. USPSTF Strength of Recommendations. 2007b. Available at:
<http://www.ahrq.gov/clinic/3rduspstf/ratings.htm#irec>
- Vernon SW. Risk perception and risk communication for cancer screening behaviors: a review. *Journal of the National Cancer Institute—Monographs*. 1999; 25:101–119. [PubMed: 10854465]
- Volk RJ, Cass AR, Spann SJ. A randomized controlled trial of shared decision making for prostate cancer screening. *Archives of Family Medicine*. 1999; 8:333–340. [PubMed: 10418541]
- Volk RJ, Spann SJ, Cass AR, Hawley ST. Patient education for informed decision making about prostate cancer screening: A randomized controlled trial with 1-year follow-up. *Annals of Family Medicine*. 2003; 1:22–28. [PubMed: 15043176]
- Welch HG. Questions about the value of early intervention. *New England Journal of Medicine*. 1996; 334:1472–1473. [PubMed: 8618589]
- Welch HG. Informed choice in cancer screening. *JAMA*. 2001; 285:2776–2778. [PubMed: 11386935]
- Welch, HG. *Maybe Not and Here's Why*. Berkeley, CA: University of California Press; 2004. *Should I Be Tested for Cancer?*
- Wolf AM, Nasser JF, Schorling JB. The impact of informed consent on patient interest in prostate-specific antigen screening. *Archives of Internal Medicine*. 1996; 156:1333–1336. [PubMed: 8651843]
- Woloshin S, Schwartz L, Welch HG. Warned, But Worse Off. *New York Times*. 2005 August 22.:A13.
- Woloshin S, Schwartz LM, Byram SJ, Sox HC, Fischhoff B, Welch HG. Women's understanding of the mammography screening debate. *Archives of Internal Medicine*. 2000; 160:1434–1440. [PubMed: 10826455]
- Woolf SH, DiGiuseppi CG, tkins D, Kamerow DB. Developing evidence-based clinical practice guidelines: Lessons learned by the US Preventive Services Task Force. *Annual Review of Public Health*. 1996; 17:511–538.
- Xu DM, Gietema H, de Koning H, Vernhout R, Nackaerts K, et al. Nodule management protocol of the NELSON randomised lung cancer screening trial. *Lung Cancer*. 2006; 54:177–184. [PubMed: 16989922]

Table 1**Ten Criteria for Effective Screening**

-
1	The disease screened has serious consequences.
2	The screening population has a high prevalence of detectable preclinical disease.
3	The screening test detects little pseudo-disease.
4	The screening test has high accuracy for detecting the detectable preclinical disease.
5	The screening test detects disease at a point in which intervention improves outcome.
6	The screening test causes little morbidity.
7	The screening test is affordable and available.
8	Treatment exists.
9	Treatment is more effective when applied before symptoms begin.
10	Treatment is not too risky or toxic.
-

Criteria from Obuchowski and colleagues (2001).