Communicating Benefits and Risks of Screening for Prostate, Colon, and Breast Cancer

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BACKGROUND: Screening for cancer has become a standard of practice in contemporary health care. Screening tests are often ordered routinely, without discussion of risks and benefits. For clinicians who want to inform patients and undertake shared decision-making, the goal of effective communication presents a number of challenges. To begin with, the probabilities to be discussed are small. For each screening test done, the chance of finding and effectively treating an early cancer is quite low. Likewise, the chance of causing harm, such as a false positive screen followed by an invasive test resulting in complications, is also very unlikely but possible. Using accurate terms that patients can understand is only the first step, however, as the decision-making process should take into account the patient's perceptions, values, and preferences. This paper briefly reviews the current state of evidence for prostate, colon, and breast cancer screening, then outlines several strategies toward effective clinical communication. The concepts of absolute risk, relative risk, and number needed to screen are reviewed. Natural frequency presentation, a relatively new method for portraying benefits and harms, is introduced and encouraged, as recent evidence suggests that natural frequencies are better understood and are more concordant with patients' values than alternative formats.

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The ethical principle of autonomy requires that physicians and other health care professionals allow patients to make their own health care choices.[1] Emergence of the biopsychosocial model,[2] combined with the twin evolutions of evidence-based medicine[3] and shared decision making,[4-6] have provided unprecedented opportunities and challenges to contemporary clinical practice. Nowhere is this more complex and portentous than in the area of cancer screening. Complex because cancer screenings have costs and risks as well as benefits, about which the evidence is substantive—yet incomplete. Portentous because cancer is an emotionally laden disease with devastating consequences. It is not so surprising, then, that the United States Preventive Services Task Force (USPSTF) revised breast cancer screening guideleines[7] released in November 2009 were met with widespread confusion and considerable public and political pushback.

Effective cancer screening must (1) be able to find malignancies early enough for treatments to be effective and (2) yield more benefit than harm when applied to the targeted population. There is increasing agreement that benefits and harms should be evaluated from the patient's perspective and that health-related quality of life should be considered along with years of life saved. Incorporating these subtleties in a shared decision-making framework requires both an understanding of the evidence and a means of effectively communicating this information.

It is now clear that mass screening leads to harms as well as benefits. For example, the ongoing Prostate, Lung, Colorectal, and Ovarian (PLCO) trial is testing transvaginal sonograms and serum cancer antigen 125 (CA-125) for ovarian cancer, chest radiographs for lung cancer, flexible sigmoidoscopies for colon cancer, and digital rectal examinations and serum prostate-specific antigen (PSA) for prostate cancer.[8] A 2009 article summarizing data from the first 68,436 participants reports that, "After 14 tests, the cumulative risk of having at least one false-positive screening test is 60.4%…for men and 48.8%…for women."[9] High false positive rates lead not only to

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emotional and economic burden but also the adversities that result from follow-up testing. The PLCO report tells us that the "cumulative risk… of undergoing an invasive diagnostic procedure prompted by a false-positive test is 28.5%…for men and 22.1% for women."[9] While rates and consequences of complications are not provided, it is clear that even if benefits are proven, harms will need to be considered. The next few paragraphs will summarize what we know about the benefits and harms of prostate, colon, and breast cancer screening.

Prostate Cancer Screening

The rationale for PSA screening is understandable. Prostate cancer is a leading cause of morbidity and mortality for men.[10-12] Most prostate cancer is slow growing, providing time and opportunity for early detection and intervention. There is some evidence for effectiveness of treatments such as surgery,[13-15] radiation, and chemotherapy.[13-17] For many years, PSA testing has been advocated as a screening tool.[18] PSA screening, however, is controversial. This controversy results from lack of convincing evidence regarding the effectiveness of either PSA screening or prostate cancer treatment, from high false positive detection rates, and from the substantive morbidity that accompanies invasive testing and treatment following a positive PSA screen.[19-23]

The 2007 Cochrane review reported on the two existing randomized controlled trials, noting "methodological weaknesses" and "high risk of bias," concluding that "There is insufficient evidence to either support or refute the routine use of mass, selective, or opportunistic screening compared to no screening for reducing prostate cancer mortality."[20] Following a similar line of reasoning, the USPSTF in August 2008 released its report on Screening for Prostate Cancer,[24] concluding that "current evidence is insufficient to assess the balance of benefits and harms of prostate cancer screening in men younger than age 75 years" and recommending "against screening for prostate cancer in men age 75 years or older."[24]

In the 3 years since those reviews, new evidence has emerged. The PLCO trial randomized 76,693 men in 10 US centers to either annual PSA screening or usual care.[25] After 7–10 years of follow-up, there were 2,820 prostate cancers found with screening, versus 2,322 in the control group.[25] The mortality trend favored no screening, with 92 prostate cancer deaths in the screened group, compared to 82 among controls.[25] A second study, the European Randomized Study of Screening for Prostate Cancer (ERSPC) randomized 267,994 men ages 50 to 74 years to PSA screening versus control.[26] A 2009 interim report did not claim overall benefit. However, a subgroup analysis on men ages 55 to 69 years reported, "The rate ratio for death from prostate cancer in the screening group, as compared with the control group, was 0.80 (95% confidence interval 0.65 to 0.98; adjusted P=.04). The absolute risk difference was 0.71 death per 1,000 men. This means that 1,410 men would need to be screened, and 48 additional cases of prostate cancer would need to be treated to prevent one death from prostate cancer."[27] These trials continue, with final results pending.

Colon Cancer Screening

Colorectal cancer is a high incidence neoplasia with considerable morbidity and mortality burden.[28-30] Screening is potentially justified because (1) most colorectal cancer is slow growing, providing opportunity for discovery before metastasis and (2) surgical and chemotherapeutic treatments have some proven benefit.[31,32] While fecal occult blood testing, double-contrast barium enema, flexible sigmoidoscopy, and colonography (virtual colonoscopy) have all been advocated,[32-34] direct optical colonoscopy is generally considered the gold standard.[35-37] This conclusion is based on a chain of reasoning and not direct evidence, as no large randomized trial has directly compared colonoscopy to not screening.[35] Mortality benefit was shown in four trials comparing fecal occult blood testing (FOBT) against no screening, with evidence suggesting a 15% relative risk reduction in colorectal cancer mortality, compared to no screening.[38] Direct comparisons of colonoscopy to FOBT show higher sensitivity and specificity for colonoscopy. Therefore, it is concluded that colonoscopy must be effective, as it is better than FOBT, which was shown to reduce mortality.[36]

In October 2008, the USPSTF released its most recent report, Screening for Colorectal Cancer.[39] This report recommended "screening for colorectal cancer using fecal occult blood testing, sigmoidoscopy, or colonoscopy in adults, beginning at age 50 years and continuing until age 75 years."[39] The USPSTF report did not endorse colonography or fecal DNA testing, but did discuss the evidence,[39] which has changed only slightly since that report was issued.[40] Burdens of colonoscopy include discomfort, loss of time, monetary costs, and risks of the procedure. The 2008 USPSTF report estimates that, for every 10,000 colonoscopies done, there are 3.8 bowel perforations and 12.3 major bleeds.[39] Overall, the rate of "serious harms," including perforation, bleed, hospitalization, or death, is "2.8 per 1,000 screening colonoscopies." Risks of sigmoidoscopy are lower, with the risk of serious harms estimated at 3.8 per 10,000 procedures.[39]

Breast Cancer Screening

Breast cancer is a leading cause of mortality and morbidity for women.[41-44] Surgery, chemotherapy, and radiation treatments can be effective, depending on stage of cancer and other factors.[45,46] Effectiveness of screening mammography has been tested in a number of trials, several of which have reported positive results. For example, the Swedish trials randomized 42,283 women to mammography screening or control. After 15.8 years of follow-up, the authors reported "a significant 21%

reduction in breast cancer mortality (RR=0.79, 95% CI 0.70–0.89)."[47] As a second example, the Canadian National Breast Screening Study enrolled 89,835 women and reported results separately for women who were ages 40–49 and 50–59 at study entry.[48,49] For both groups, mammography "detected considerably more node-negative, small tumors than usual care, but it had no [statistically significant] impact on the rate of death from breast cancer." As a final example, the UK's Age trial randomized 160,921 women ages 39 to 41 to annual mammographic screening or usual care.[50] After 10 years of follow-up, these investigators reported a nonsignificant (*P*=.11) 17% relative risk reduction in breast cancer mortality.[50]

With data from several large trials available, systematic review or meta-analysis is the most appropriate way to synthesize findings. Using these methods, the 2006 Cochrane report concludes: "Based on all trials, the [relative risk] reduction is 20%, but as the effect is lower in the highest quality trials, a more reasonable estimate is a 15% relative risk reduction. Based on the risk level of women in these trials, the absolute risk reduction was 0.05%. Screening also leads to over-diagnosis and overtreatment, with an estimated 30% increase, or an absolute risk increase of 0.5%."[51] The November 2009 USPSTF report[7] and accompanying articles[52,53] provide similar conclusions. This report recommends "biennial screening mammography for women aged 50 to 74 years,"[7] reversing earlier recommendations for annual screening starting at age 40.[52,53] The new recommendations also say that "The decision to start regular, biennial screening mammography before the age of 50 years should be an individual one and take patient context into account, including the patient's values regarding specific benefits and harms."[7]

Communicating Benefits and Risks of Cancer Screening

Weighing the probabilities and magnitudes of benefits and harms is central to rational informed decision making. Nevertheless, communicating risks and benefits involved with cancer screening presents several significant challenges. Understanding best current evidence is only the first step. During a clinical encounter, the clinician describes what the intervention is and why it should be considered. This involves a quantitative portrayal of good results (chances of finding a cancer, chances of cure once a cancer is found) and bad results (chances of missing cancers, chances of false positive results leading to invasive procedures, chances of invasive procedures leading to complications). This conversation is unavoidably complicated by uncertainties with each step of screening and follow-up. What can result is an overload of information, obscuring the most salient points. To avoid overload (and to stay on schedule) communication strategies must be targeted and simplified.

Portrayals of probability can include qualitative (descriptive) and/or quantitative (numeric) terminology.[54-57] Commonly used presentation formats include relative risk, absolute risk, and number needed to screen to achieve benefits or to cause harms. Relative risk reduction refers to the degree to which the risk of a bad outcome in the screened group compares to the risk in the non-screened group. For example, the Cochrane and USPSTF reviews suggest that with regular mammographic screening, women ages 50 to 74 will be 15% to 20% less likely to die from breast cancer than if they had no screening.[7,51] Absolute risk reduction, on the other hand, refers to the actual difference between risks of dying from breast cancer, which are less than 1 in 200 for most women, during a typical 10-year screening period. As an example, let's say that 33 of 10,000 women (0.33%) not screened die of breast cancer, compared to only 28 of 10,000 (0.28%) who are screened. In this case the relative risk reduction is (0.33%–0.28%)/0.33%=15%, and the absolute risk reduction is 0.33%–0.28%=0.05%. The number needed to screen to achieve one less death from breast cancer is the inverse of 0.05% or 2,000 women. Similar evidence and reasoning can show that the absolute risk of false diagnosis or unhelpful treatment is about 0.5%, so the number needed to harm is about 200.

While such descriptors and explanations may be useful in certain contexts, the effectiveness of communication may diminish when the clinician attempts to portray multiple statistical concepts in the same conversation. For example, a discussion of cancer screening could include descriptors of the test (sensitivity, specificity, positive and negative predictive value), of the trial-based evidence (relative and absolute risk reduction, number needed to screen to benefit and harm, complication rate of invasive testing), and of what this could mean to the patient (dying from cancer, undergoing surgery, radiation, or chemotherapy; having side effects related to treatment). What is required is an approach that presents the most salient information to the patient in terms that can be easily understood, to reach toward the goal of well-informed shared decision-making.

One such promising approach is called "natural frequency presentation."[58-60] Natural frequencies portray the chances of an event (benefit or harm) occurring in both screened and non-screened populations, using an appropriately sized cohort as the reference group. The 2006 Cochrane report uses a natural frequency approach when it states, "This means that for every 2,000 women invited for screening throughout 10 years, one will have her life prolonged. In addition, 10 healthy women, who would not have been diagnosed if there had not been screening, will be misdiagnosed as breast cancer patients and treated unnecessarily."[51]

This method uses one discrete reference group to portray both risks and benefits. It eliminates the psychological magnification that occurs when risks and benefits are presented in relative terms and avoids the distortions that occur when different size reference groups are used to portray different kinds of information.[61-66] Most importantly, it puts both risks and benefits in an understandable context, allowing individuals a more natural framework for assessing the probability of benefits and harms occurring as a result of their choice to screen or not screen. Examples of various methods of risk/benefit communication are shown in Table 1.

Two studies published in 2009 lend support to the natural frequency approach. In one, Carling and colleagues randomized 2,978 participants recruited via Internet to one of six approaches to communicating potential benefits of statins for preventing heart disease.[67] Presenting information as natural frequencies led to higher levels of self-reported

Table 1: Different Ways of Portraying Benefits and Harms of Cancer Screening

	Prostate Cancer	Colon Cancer	Breast Cancer
Descriptive	"A large ongoing American trial has found no benefit to PSA screening. While not statistically significant, prostate cancer mortality was actually higher in those who were randomly assigned to PSA screening."	"Colonoscopy is better at finding early colon cancer than fecal occult blood screening, which has been shown to reduce colon cancer mortality." "Sigmoidoscopy is safer than colonoscopy but may miss lesions beyond its reach."	"There is more evidence for mammography than for any other cancer screening test." "Current evidence suggests that there may be more harm than benefit from screening average risk women less than 50 years old."
Conventional Statistical Presentation	"An ongoing European trial has reported that for men aged 55 to 69 years old, PSA screening may reduce prostate cancer mortality by 20%." (relative risk reduction) "An ongoing European trial has reported that men aged 55 to 69 years might lower their absolute risk of dying from prostate cancer by 0.07% with PSA screening." (absolute risk reduction) "A large European trial found that for every 1,400 men aged 55 to 69 screened with PSA, one would have his life prolonged, and 48 men would be treated unnecessarily." (number needed to screen, with benefits and harms)	"Fecal occult blood screening has been shown to reduce colon cancer mortality by about 15%." (relative risk reduction) "Regular colonoscopy screening starting at age 50 may reduce the risk of dying from colon cancer from 3% to 2.5%." (absolute risk reduction) "For every 200 men undergoing regular colonoscopy screening, as many as one will have a cancer found and cured." (number needed to treat) "For every 360 colonoscopies done, one person will experience a serious harm, such as perforation, bleed, hospitalization or death." (number needed to harm)	"While not all mammography trials demonstrate benefit, putting all the evidence together suggests that women ages 50 to 74 may reduce breast cancer mortality risk by 15 to 20%." (relative risk reduction) "Women ages 50 to 74 getting regular mammographic screening for 10 years may reduce their absolute chance of dying from breast cancer by approximately 0.05%." (absolute risk reduction) "For every 2000 women getting regular mammographic screening, one will have her life prolonged, and 10 women will be diagnosed as breast cancer patients and treated unnecessarily." (number needed to screen, with benefits and harms)
Natural Frequency	"Without screening, over 10 years, approximately 40 of 10,000 men ages 55 to 69 would be expected to die from prostate cancer. With regular PSA screening, only 33 would be expected to die from prostate cancer and seven lives would be prolonged. To achieve these benefits, more than 300 would need to be treated, and many would have side effects, such as impotence or incontinence."	"Without screening, approximately 30 of every 1,000 adults will die of colorectal cancer. Regular screening with colonoscopy beginning at age 50 may reduce this risk, so that only 25 would die of this disease. However, for every 1,000 colonoscopies performed, at least two people will have serious side effects, such as intestinal perforation, bleeding, hospitalization, or even death."	"Without screening, approximately 30 of 1,000 women over age 40 can be expected to die from breast cancer. With regular mammography, six lives will be prolonged, so only 24 women will die of breast cancer. However, regular screening those 1,000 women will lead to more than 2,000 false positives results, and 150 women will receive unnecessary biopsies."

preference, understanding, satisfaction, and confidence in decision-making.[67] In the other study, Galesic and Gigerenzer used a conventional educational testing approach, assessing ability to impart information regarding potential benefits of screening for diabetes.[58] Presenting information as natural frequencies rather than as conditional probabilities allowed 58% of elderly participants to "give the right answer" compared to 18% of those given the same information as conditional probabilities (P=.001).[58] These authors reported that their study "demonstrated for the first time that elderly and low-numeracy people benefit from natural frequencies."

Discussion

Decades of research across multiple disciplines has shown that individual health values vary tremendously across populations.[68-71] Various approaches have demonstrated that people interpret and value benefits and harms in highly divergent manners.[72-75] Given this heterogeneity in health values, shared medical decision making[4-6] is now considered an essential element of high-quality health care.[76-80] Applying standardized approaches without regard to individual values violates the principle of autonomy and puts patients at risks for harms they would have avoided had they been informed.

The ethical principle of patient autonomy compels us to present complex information in manners that facilitate understanding, minimize bias, and allow patients to make the best possible decisions regarding their health care. The discussions around cancer screening are particularly complex and may require better techniques than we currently have at our disposal. Patient information pamphlets, well-designed Web sites, and graphical displays of risks and benefits may be required. Nevertheless, it is the clinical encounter where most decisions are made, and verbal communication is still the foundation of doctor-patient interaction. Although certainly not a panacea, natural frequency presentation offers a clear and coherent means of presenting statistical information and can be advocated and incorporated into evidence-based and patient-oriented clinical practice.

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