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False-Positive Cancer Screens and Health-related Quality of Life

KEY WORDS

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By design, screening tests are imperfect—unresponsive to some cancers (false negatives) while occasionally raising suspicion of cancer where none exists (false positives). This pilot study describes patients' responses to having a false-positive screening test for cancer, and identifies screening effects on health-related quality of life (HRQoL). The pilot findings suggest issues important for incorporation in future evaluations of the impact of screening for prostate, lung, colon, or ovarian (PLCO) cancers. Seven focus groups were conducted to identify the nature and meaning of all phases of PLCO screening. Minnesota participants in the Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial who had completed screening, with at least 1 false-positive screen, participated ($N = 47$). Participants' reactions to abnormal screens and diagnostic work-ups were primarily emotional (eg, anxiety and distress), not physical, and ultimately positive for the majority. Health distress and fear of cancer and death were the major negative aspects of HRQoL identified. These concepts are not typically included in generic HRQoL questionnaires like the SF-36, but are highly relevant to PLCO screening. Clinicians were regarded as underestimating the discomfort of follow-up diagnostic testing. However, relief and assurance appeared to eventually outweigh the negative emotions for most participants. Implications for oncology nurses include the need to consider the emotional consequences of screening in association with screen reliability and validity.

This article describes patients' responses to the experience of having a false-positive screening test for cancer. Focus-group methodology was used to uncover themes not captured by standard, generic questionnaires used to measure general

health-related quality of life (HRQoL) like the SF-36.¹ This pilot study was conducted to provide information on measuring HRQoL for incorporation into future cost-effectiveness studies within the Prostate, Lung, Colorectal and Ovarian Cancer

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Screening Trial (PLCO). Study findings on patients' experience of having a false-positive screening test for cancer have implications for nursing practice and research addressing HRQoL.

■ Background

Prostate, lung, colorectal, and ovarian cancers account for half of all diagnosed cancer cases and half of all cancer deaths in the United States annually.² Reis et al³ provide age-adjusted data for the United States, 1996–2000. Lung cancer is the leading cause of cancer mortality in men and women at 56.8/100,000. Prostate cancer is the second most common cause of cancer mortality in men, with a mortality rate of 32.9/100,000. Colorectal cancer mortality is estimated at 21.2/100,000; it is the second most common cause of cancer mortality affecting both men and women. Ovarian cancer mortality is estimated at 8.8/100,000. There is substantial variation by race in cancer incidence, eg, African American men have the highest incidence of prostate and lung cancers, Alaskan native men and women have the highest incidence of colorectal cancer, while white women have the highest incidence of ovarian cancer.⁴

It is unclear whether screening for prostate, lung, colorectal, and ovarian cancers will produce a survival benefit. Clinical trials on the reduction of cancer mortality achieved with screening will address this issue. Currently in progress are the PLCO in the United States and the Randomized Study of Screening for Prostate Cancer (ERSPC) in Europe. Substudies to the PLCO have also been initiated to address questions of cost-effectiveness. (For a history of the PLCO, see Gohagen et al.⁵)

Cancer screening may have benefits that are not captured by mortality measures. Early detection and prompt treatment may improve functioning and quality of life, even if it does not extend life. Alternatively, cancer screening may produce side effects including short-term effects such as pain, fear of embarrassment, and anxiety about screening outcomes^{6–8} or long-term effects such as disability from follow-up, invasive diagnostic procedures, and cancer surgery.⁹ In the PLCO some cancer screens have minimal patient burden (eg, chest x-ray for the lung screen). In contrast, other screens may cause discomfort or distress, such as the flexible sigmoidoscopy used for the colon screen, or the transvaginal ultrasound used for the ovarian screen. These issues become important for public policy, if the effect of screening is a moderate to small reduction in cancer yet large numbers of people are being screened and experiencing detrimental effects to HRQoL.

Generic HRQoL measures may not be sufficiently sensitive to detect any effects of screening in healthy older adults. Yet, such effects (eg, anxiety in response to screening or anger in response to a false-positive screening test) might trigger negative emotions or physical consequences sufficient to cause non-compliance with future screens or treatments.

■ Study Purpose

A pilot study was conducted to examine patients' perspective on cancer screening in the PLCO to provide insights for

measuring screening-specific effects on HRQoL in a subsequent larger evaluation effort. This article explores the meaning of the cancer screen experience, particularly the false-positive experience, to propose screening-specific questionnaire items that could augment a standardized, generic HRQoL questionnaire such as the SF-36^{1,*} for a cancer screening trial.

■ Methods

Focus group methods¹⁰ were used to structure discussions with PLCO participants who had completed screening, and had at least 1 false-positive screen, but were negative for cancer. The eligibility criteria were persons whose screen results were "abnormal and suspicious" and were referred for a diagnostic work-up, but were ultimately found cancer-free (Table 1). These persons were expected to have experienced the most inconvenience and to be most upset among those screened, with the exception of the true positives. All participants being currently treated for any cancer or with debilitating disease were excluded.

Data Collection

Invitations were mailed to 67 individuals. Seven focus groups of 5 to 12 individuals were conducted. Participants were organized by type of false-positive screen and gender; the groups were internally homogeneous to foster relaxed, in-depth, and open dialogue. Although focus group methodology suggests recruitment of subjects who can easily articulate their experience, this project invited everyone who met the eligibility criteria. All participants were mailed thank-you letters, a \$25.00 subject incentive, and mileage reimbursement after participation.

✿ **Table 1 • Additional Eligibility Criteria***

PLCO Cancer Screen	Criteria
Prostate screen	• Prostate-specific antigen (PSA) greater than 4.0/mL and negative results for a biopsy
Lung screen	• Abnormal and suspicious screening chest x-rays and negative follow-up computerized tomographic (CT) scan
Colorectal screen	• A polyp greater than or equal to 0.8 cm and a negative follow-up colonoscopy
Ovarian screen	• Abnormal and suspicious transvaginal ultrasound with a follow-up negative for cancer

*PLCO indicates Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial.

*The SF-36 was selected as the core measure of HRQoL after consideration of many instruments because of its brief yet valid and reliable set of standardized measures that assess a comprehensive core of HRQoL domains. Additionally, it has been used with healthy and ill persons, and with persons in the age groups of the PLCO.

The focus group utilized discussions with skilled moderators (R.A.K. or P.M.M.) using predetermined questions. Discussion topics included the experience of the first screen; wait for screen results; notification of the abnormal screen; medical evaluation to an abnormal screen; final outcome of the diagnostic work-up; and the meaning of the entire experience. Discussions were augmented with written worksheets and posters to aid less verbal participants. The group facilitator would explain a worksheet and ask participants to independently complete it. After all participants completed a given worksheet the facilitator invited comments from anyone who wished to share what he/she had written.

One worksheet addressed the various categories of life potentially affected by the screen. Representative life categories were

selected from the Sickness Impact Profile¹¹ and augmented by investigators' judgments. The list included categories such as emotions, reasoning and problem solving, and spirituality, as detailed in Table 2. A second worksheet displayed a timeline of the various phases of screening and asked participants to report their feelings in association with each phase of screening, also detailed in Table 2. The third worksheet employed a visual analog scale to assess participants' quality of life before enrollment in the PLCO, after learning of a suspicious abnormal screen, and today. Finally, a wall poster was displayed at all focus groups as an additional visual aid for less verbal participants. It identified a list of potential feelings associated with screening using semantic differential (eg, nervous-calm, happy-sad) as noted in Table 2. Discussions were taperecorded and transcribed.

 **Table 2 • Focus Groups Aids***

Focus Group Aids	Content
<p>Written worksheet 1</p> <p>Life categories potentially affected by the cancer screen; adapted from the Sickness Impact Profile¹¹</p>	<ul style="list-style-type: none"> • Emotions • Reasoning and problem solving • Spirituality • Sexuality • Interactions with family and friends • Sleep • Usual exercises or activities • Usual daily work and household management • Dietary practices • Smoking habits • Alcohol use • Prescription drug use • Usual leisure time activities
<p>Written worksheet 2</p> <p>Timeline of the phases of PLCO cancer screening and participants' associated feelings; developed by investigators</p>	<ul style="list-style-type: none"> • The first screen • Waiting for the screen result • Notification of the abnormal, suspicious screen • Medical evaluation in response to the abnormal screen • Final outcome of the diagnostic work-up • The meaning of the entire screen process
<p>Written worksheet 3</p> <p>Visual analog scale (VAS) to assess participants' quality of life at various stages of PLCO screening; adapted from the EuroQoL¹²</p> <p>Wall poster identified a list of 50 potential feelings associated with PLCO cancer screening as an aid for less verbal participants</p>	<ul style="list-style-type: none"> • Before enrollment in PLCO • After learning of a suspicious abnormal screen • Today • Curious, interested • Calm, serene, prayerful, appreciative, grateful • Comforted, supported, relieved, reassured • Angry, hostile, bitter, resentful • Irritated, annoyed, agitated, embarrassed • Happy, upbeat, elated, excited, energized, hopeful, positive, joyful, revitalized, vibrant, enthusiastic • Anxious, fearful, fretful • Unsure, confused, puzzled • Depressed, distressed, upset, unhappy, discouraged, saddened, drained • Lonely, isolated • Confident • Unaffected, indifferent, resigned, unconcerned

*PLCO indicates Prostate, Lung, Colorectal and Ovarian cancer Screening Trial.

Data Analysis

Transcripts were analyzed by coding data for common themes. Two co-investigators (P.M.M. and C.R.G.) independently evaluated the focus group transcripts and in discussion resolved any differences in interpretation to address reliability concerns.¹³

■ Results

Focus Group Participants

Seven focus groups were conducted; 47 individuals (46/67 = 70% response rate) participated. There were 2 groups for prostate screens ($n = 16$), 2 groups for lung screens (6 males, 6 females) and colorectal screens (9 males, 7 females), and 1 group for ovarian screens ($n = 3$).

Focus Group Discussion Themes

Participants' reactions to suspicious, abnormal screens and diagnostic work-ups were primarily emotional rather than physical. Individual characteristics such as older age, prior screening experience, tragic life experiences, and screen-specific factors (eg, use of a television monitor to visualize colorectal screening), and positive patient-provider relationships appeared to mitigate negative reactions to screening. Participants' reactions to a false-positive screening test were generally positive, and included emotional, spiritual, intellectual, and behavioral dimensions.

INITIAL REACTIONS TO SCREENING

While reactions to the abnormal screens varied, many participants expressed mild anxiety, worry, apprehension, and surprise. A minority expressed indifference or curiosity; a few expressed fear and anger. Anxiety—the most commonly expressed emotion—is exemplified in the comments below from men with false-positive screening tests for prostate cancer.

You know, I've had friends that died of cancer, relatives too. You're thinking, geez, what if I've got it? I was rattled—a little bit, not a whole lot. I mean I'm not scared to death of it, but, man, it's there and you think about it quite a bit.

I think as your PSA score changes then you get more anxious. As long as you stay in the normal range, it's just life as usual. But, if you see a change, that's when I think it's significant. I mean I didn't lay awake at night, but I was anxious to get that card (ie, PSA results).

Alternatively, some individuals denied worrying, and their lower levels of anxiety appeared associated with past experience with screening or observing screening on a television monitor.

Participants' reactions to their screening varied by the type of screen. Women described experiences with the ovarian screen as noneventful, causing only mild discomfort and anxiety; in comparison to childbirth the screen was “nothing.” In contrast, colorectal screens caused much more distress—including the discomfort and embarrassment of the flexible

sigmoidoscopy, or the anxiety associated with having friends who had died from colon cancer. Short-term physical reactions to the colorectal screen included abdominal gas, cramping, and diarrhea.

LEARNING THE ABNORMAL RESULT

It was frequently difficult for participants to distinguish the screening procedure from their knowledge of the screening outcome as participants sometimes learnt that their results were abnormal or suspicious during screening (eg, participants gleaned clues while observing a colonic polyp on the television monitor), despite caution exercised by PLCO nurses not to disclose suspected findings.

Written notice of an abnormal, suspicious screen triggered more anxiety, apprehension, and surprise. Some expressed a greater awareness of mortality saying, “don't leave your wife in a mess,” “line up your ducks,” “check your will,” and “get your house in order.” A few described being curious; some expressed fear or anger. Factors that appeared to mitigate distress included older age, significant life experiences that served as a benchmark for greater distress (eg, childbirth, experience in a world war), the support of others, keeping active, having spiritual faith, and feelings of tolerance for any variations in medical practice.

Participants who had experienced serious health problems, their own or those of family members, appeared relatively more sanguine about abnormal screens.

My urologist eventually discovered my (prostate) biopsy was benign, but I was always anxious, more anxious about my heart condition, because I had a triple bypass about 12 years ago. My father died much younger than me and it's in the family. So, my heart was always more of a concern for me, but I know that cancer is possible...

Individuals' tolerance for variations in screen results or ambiguity regarding results appeared associated with distress as described below. One man reported prior experience with screening, involving fluctuating prostate-specific antigen (PSA) scores, followed by a benign biopsy, and subsequently elevated PSA scores.

It could become cancerous I suppose, but I'm not terribly exercised over that possibility. If I have to have that operation, it would be o.k. You know, I'm not sitting on pins and needles.

Another man who lacked experience with cancer screens said (after receiving notice of his abnormal prostate screen):

...I called my physician right away and asked how come he hadn't checked my PSA before when I saw him for a physical, cause he had said my prostate was enlarged. He said there wasn't any reason to check it. He asked me about the numbers on the letter from the PLCO so I told him. He said, 'We don't do it the way they do at the University.' I say 'what do you mean?' Well, which one are you going to believe? I was kind of disgusted with him. I belong to an HMO so I went to see if I could get another doctor and I did. I was kind of up on end about it, because it should have been caught sooner...

A third man, who lacked experience with serious illness, was younger than other focus group members (early 60s), divorced, and the only participant who reported dating, expressed marked worry about cancer and the possible side effects of prostate cancer surgery (eg, impotence and incontinence). He knew someone whose surgery had caused “a ton of problems,” and said his own elevated PSA had “put a shroud on him,” creating feelings of fear of cancer and death, making him feel like “his life was on hold.”

FOLLOW-UP TESTING

Follow-up diagnostic procedures caused concern. Participants' reactions ranged from calling it a “non-event” to feeling intense anxiety and awareness of one's mortality, and pain (specific to prostate, ovarian, and colorectal follow-ups). Factors mitigating distress included confidence in and good communication with medical professionals, a positive mental attitude, and spiritual faith.

Some participants' anxiety appeared associated with an increased awareness of mortality. One woman reported anxiety attacks before her colorectal work-up, and another reported that she did a “death clean” (ie, straightened up her personal items in anticipation of death and the expectation of others sorting through her most personal possessions) the night before the follow-up on her abnormal lung screen. She also reported night-time ruminations about whether to be cremated or buried, and keeping busy during the day to avoid thinking of a potential cancer diagnosis.

Maintaining a positive mental attitude was an important coping strategy for many.

I think no matter how down you are, the right attitude is that we're somehow going to win this battle. You lose right at the start if you are discouraged or indifferent. I think nowadays I got one day at a time.

Participants' relationship with their physicians appeared to greatly influence their reactions to the diagnostic follow-up of their abnormal screens.

I think it's terribly important that you have confidence in your doctor; if you don't you're going to be in doubt all the time. ... this is the first guy I really had confidence in ... he kept me totally informed of what was happening and when he said, 'you're ok,' I believed him...

In contrast, 2 women had suspicious abnormal ovarian screens and subsequently had surgery for removal of ovarian cysts. Although their negative biopsies were a source of pleasure and reassurance, both women reported that their primary care (male) physicians unduly minimized their postoperative recovery. One woman stated:

I was told the procedure was minor, and recovery would only take a few days, but I had bleeding for more than two weeks...

AFTER THE NEGATIVE DIAGNOSIS

Participants' reactions being negative for cancer were generally a source of joy, relief, gratefulness, and an increased awareness

of their mortality. For a minority there were questions about the need for future screening after the PLCO. Some reported their resolve to engage in healthy behaviors (diet, exercise), and appreciation for life was strengthened.

There were intellectual, social, and behavioral dimensions to participants' reactions to their negative findings for cancer. Intellectual reactions included ongoing questions about the reliability and validity of the screens, and time spent searching the Internet or clipping news articles on screening. These participants had ongoing concerns about cancer screening and remained vigilant about their health, particularly for fluctuating PSA scores. Social reactions were revealed by participants who expressed increased appreciation for the support from family or friends throughout screening. Participants' behavioral reactions were revealed by a few who stated that they had changed their diet, started exercising or stopped smoking to improve their health as a consequence of participation in the PLCO. Some participants' experience with the PLCO appeared to positively influence their feelings of mastery for managing their health.

■ Discussion and Implications for Practice and Research

Focus group findings are limited by the small sample size, and the lack of diversity relative to race, social class, and location. Focus group participants were all white, and relatively well educated, but their race and social class reflected Minnesota's PLCO participants. The PLCO participants are a self-selected group having volunteered for participation in the clinical trial. Many perceive the screenings to be a part of their commitment to taking care of their health; several describe the free screenings to be a “good deal.” Such perspectives may make these volunteers more tolerant of any stresses associated with screening relative to the general population.

Focus group findings have potential implications for clinical practice and for development of a questionnaire for evaluating HRQoL in cancer screening studies. The short-term effects of an abnormal suspicious screen appeared primarily emotional and included anxiety and health worry for many, and fear of death and dying for some. Some participants expressed pain and embarrassment with the flexible sigmoidoscopy or the preparation for a colon biopsy. Some participants expressed pain with the prostate biopsy. The long-term effects of a false-positive screening test appear to be primarily relief and reassurance, and an increased awareness of one's mortality. Participants were grateful for being cancer free and having had the opportunity to be screened. There were no findings to suggest participants experienced cancer “labeling” or reduced their compliance with screening in association with a false-positive screening test.

If such findings are replicated in studies with a larger and more diverse patient population, clinicians conducting screening might wish to discuss with patients the emotional consequences of screening in association with issues of screen reliability and validity. Such issues could also be addressed in

patient education materials, and reinforced by nurses working with patients throughout the screen process.

Findings relevant to questionnaire design suggest that cancer screening touches aspects of HRQoL not routinely assessed in generic health profiles like the SF-36. It is recommended that a generic HRQoL questionnaire that addresses mental health, such as the SF-36, should be augmented with screen-specific measures of health distress (ie, feeling fearful about one's general health), fear of cancer and death, and intrusive thoughts of illness. Inclusion of screen-specific measures should increase the sensitivity of the health profile to the impact of screening, whether it is used as a purely descriptive measure or converted into an index for cost-utility analysis and economic evaluations. Given the study's limitations (ie, a small sample with participants who were white and well educated) additional research is needed to replicate this effort in a larger and more diverse sample. Quantitative research is also needed to determine if factors like spiritual faith, satisfaction with healthcare, and social support mediate the impact of screening on HRQoL. Additionally, questions exist about the timing of measurement for evaluation of HRQoL screening effects, as it appears that the effects on patients change with time. While the immediate effects for many were anxiety and a decline in HRQoL, with time most patients viewed the experience positively. Research is needed to evaluate when to measure HRQoL in association with screening and diagnostic work-ups and how best to distinguish between true changes in HRQoL and problems in measurement reliability.

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