The Impact of a Suspicious Prostate Biopsy on Patients' Psychological, Socio-behavioral, and Medical Care Outcomes

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OBJECTIVE: To evaluate the psychological, socio-behavioral, and medical implications of apparently false-positive prostate cancer screening results.

METHODS: One hundred and twenty-one men with a benign prostate biopsy performed in response to a suspicious screening test (biopsy group) and 164 men with a normal prostate-specific antigen (PSA) test result (normal PSA group) responded to a questionnaire 6 weeks, 6 and 12 months after their biopsy or PSA test.

RESULTS: The mean ($\pm$ SD) age of respondents was 61 $\pm$ 9 years (range, 41 to 88 years). One year later, 26% (32/121) of men in the biopsy group reported having worried "a lot" or "some of the time" that they may develop prostate cancer, compared with 6% (10/164) in the normal PSA group ($P<.001$). Forty-six percent of the biopsy group reported thinking their wife or significant other was concerned about prostate cancer, versus 14% in the normal PSA group ($P<.001$). Medical record review showed that biopsied men were more likely than those in the normal PSA group to have had at least 1 follow-up PSA test over the year (73% vs 42%, $P<.001$), more likely to have had another biopsy (15% vs 1%, $P<.001$), and more likely to have visited a urologist (71% vs 13%, $P<.001$).

CONCLUSION: One year later, men who underwent prostate biopsy more often reported worrying about prostate cancer. In addition, there were related psychological, socio-behavioral, and medical care implications. These hidden tolls associated with screening should be considered in the discussion about the benefits and risks of prostate cancer screening.

KEY WORDS: prostate biopsy; prostate cancer; screening.
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Despite controversy over the effectiveness of screening for prostate cancer,[1] the practice is widespread in the United States.[2] The usefulness of the prostate-specific antigen (PSA) test as a screening tool for prostate cancer has recently been called into question by an early proponent of the test.[3] Stamey and colleagues examined 1,317 consecutive radical prostatectomies between 1983 and 2003, and showed that serum PSA was related to prostate cancer 20 years ago, but in recent years was only related to benign prostatic hyperplasia. Given the uncertainty about the potential benefits of prostate cancer screening, it is imperative to understand the potential for risks (including psychological distress) associated with screening. Previous work[4] demonstrated that many men with an apparently false-positive prostate cancer screening test, meaning a suspicious screening test followed by a benign biopsy (cautiously called "false positive" because some of these men may have had a false-negative biopsy result), suffered negative psychological effects about 6 weeks later. In this study, we evaluated the longer-term psychological and other effects of an apparently false-positive prostate cancer-screening test.

METHODS

Study Sample

A prospective cohort of men recently screened for prostate cancer was assembled between August 2001 and September 2002 from the primary care practices of Massachusetts General Hospital, Brigham and Women's Hospital, and Boston Medical Center to study the psychological, socio-behavioral, and medical care of patients who were not found to have cancer after a prostate biopsy. The Institutional Review Board of each institution approved the study.

Patients were identified through weekly review of pathology reports and PSA test results. The inclusion criteria were as follows: men, aged 40 and older, living in the United States, with a primary care physician at 1 of the participating institutions, and a benign prostate biopsy performed because of a suspicious screening test (biopsy group). A normal PSA group consisted of men who had a normal PSA test (defined as <2.5 ng/mL) during the same period. Exclusion criteria were as follows: a diagnosis of prostate cancer, inability to understand English, and permission from the physician not granted; previous prostate biopsy was an additional exclusion criterion in the normal PSA group.

Study Design

After telephone contact and consent were obtained, prospective participants were mailed a brief (<10 minutes), self-administered, pretested questionnaire about 6 weeks after their benign biopsy (biopsy group) or normal screening PSA test (normal PSA group). Patients who returned the 6-week ques-

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tionnaire, which was the baseline data collection, were surveyed again at 6 months, and those who responded at 6 months were sent questionnaires at 12 months. Because of an Institutional Review Board stipulation that nonresponse after reminders be considered a refusal, patients who did not return any questionnaire were not sent further surveys. A telephone reminder and mailing to nonrespondents was employed at each time point. Please see previous publication for additional details.[4]

Response. After the initial phone contact and consent, 480 patients were deemed eligible and sent a 6-week questionnaire; 83% (239/287) in the biopsy group returned a survey and 87% (168/193) in the normal PSA group responded. One man in the biopsy group and 7 in the normal PSA group were deemed ineligible based on responses to the first questionnaire, and were excluded from analysis and further follow-up. At 6 months, 83% (139/167) of the biopsy group and 84% (194/232) of the normal PSA group returned a questionnaire. One man in each group reported being diagnosed with prostate cancer on the 6-month questionnaire, and was excluded from further analysis and follow-up. In the biopsy and normal PSA groups, 88% (121/138) and 85% (164/193), respectively, returned a 12-month questionnaire. Overall, 63% (121/193) of the original biopsy group and 57% (164/287) of the original normal PSA group returned a 12-month survey.

Responders and Nonresponders. Based on characteristics reported in Table 1 at 6 weeks, there were some differences between responders and nonresponders at 6 and 12 months. In the biopsy group, we found no difference between 6-month responders and nonresponders in these variables, and 1 difference between 12-month responders and nonresponders. Twelve-month responders in the biopsy group reported having had more PSA tests at 6 weeks than nonresponders; 8% versus 16% had 1 PSA test, 25% versus 40% had 2 to 4, 41% versus 30% had 5 to 10 and 27% versus 14% had 11 or more, $P=.04$. In the normal PSA group, at 6 months the responders were more likely to be white (90% vs 72%, $P=.007$), college educated (90% vs 74%, $P=.02$), and have had more PSA tests (14% vs 31% had 1 PSA test, 37% vs 49% had 2 to 4, 36% vs 17% had 5 to 10 and 13% vs 3% had 11 or more, $P=.007$). Twelve-month responders in the normal PSA group were older (mean age 61 vs 58, $P=.03$), more likely to be white (91% vs 78%, $P=.02$), married (80% vs 61%, $P=.004$), and college educated (91% vs 79% $P=.02$). The 12-month responders also had more PSA tests than the nonresponders (11% vs 31% had 1 PSA test,

Table 1. Baseline Characteristics of the Participants*

Characteristic	N (%)		P Value
	Biopsy Group N=167	Normal PSA Group N=232	
Mean age	61.1	59.8	P=.15
Age (y)			
< 50	16 (10)	29 (13)	P=.40
50 to 59	58 (35)	89 (38)	
60 to 69	63 (38)	77 (33)	
70 to 79	29 (17)	32 (14)	
80+	1 (1)	5 (2)	
White, not Hispanic	149 (90)	201 (87)	P=.34
Married	131 (79)	171 (74	P=.34
Education			
High school or less	31 (19)	29 (13)	P=.24
Some college or degree	69 (42)	103 (44)	
Advanced degree	66 (40)	100 (43)	
Family history of prostate cancer	23 (14)	31 (13)	P=.88
Benign prostatic hyperplasia	57 (34)	30 (13)	P<.0001
Prostatitis	38 (23)	21 (9)	P<.0001
Approximately how many prostate specific antigen tests have you had?			
1	16 (10)	35 (17)	P=.002
2 to 4	46 (29)	82 (39)	
5 to 10	61 (38)	68 (33)	
11+	38 (24)	24 (11)	
Visits to urologist over past 12 months			
0	3 (2)	179 (79)	P<.0001
1	48 (29)	28 (12)	
2+	114 (69)	21 (9)	
Overall rating of current physical health			
Excellent	49 (30)	56 (24)	P=.14
Very good	60 (36)	101 (44)	
Good	47 (28)	52 (22)	
Fair-poor	10 (6)	23 (10)	
Overall rating of current mental health			
Excellent	72 (43)	89 (38)	P=.57
Very good	56 (34)	88 (38)	
Good	33 (20)	42 (18)	
Fair-poor	6 (4)	13 (6)	

*Number for individual items vary slightly because of nonresponse.
PSA, prostate-specific antigen.

40% vs 37% had 2 to 4, 35% vs 25% had 5 to 10, and 13% vs 7% had 11 or more, P=.007).

To assess whether response was associated with any of the outcome variables we examined responders versus nonresponders at 6 and 12 months separately on 3 key psychological outcome variables (prostate cancer risk perception, worry about prostate cancer, and thinking about prostate cancer). There were no significant differences between 6-month responders and nonresponders on these 3 variables at 6 weeks. Additionally, we found no significant differences between 12-month responders and nonresponders on the 3 psychological variables at 6 weeks, or at 6 months.

Measurements

Questionnaire Development. A literature review of assessments of the psychological effects of suspicious prostate cancer screening results identified few relevant studies[5–8]; therefore, assessments quantifying the effects of suspicious mammograms were reviewed.[9–12] We conducted 3 focus groups of men who had a benign biopsy result in response to a suspicious screening test and 1 focus group of men who had a normal screening PSA test. A preliminary questionnaire was developed, and refined using in person pretesting (n=5). See previous publication for additional details.[4]

Demographics, Family History, Medical History, and Health Status. Information on age, race, marital status, education, medical history, health status, and family history of prostate cancer was collected.

Psychological Impact. Men were asked how much they had thought about prostate cancer, had worried about developing prostate cancer, what they thought was their chance of getting prostate cancer someday, and how reassured they felt as a result of their most recent PSA test.

Socio-behavioral Impact. Men were asked how much they talked with their wife or significant other about prostate cancer, and how much they thought their wife or significant other was concerned about them developing prostate cancer. Men were also asked about knowledge seeking related to prostate cancer—reading books, magazine or newspaper articles, or searching the Internet for information, and how well informed they felt about prostate cancer.

Medical Care. We performed a medical record review to document how many PSA tests and prostate biopsies the men in our study had over the 1 year of follow-up. Men were also asked how many times they had visited or called their primary care provider and urologist over the year.

Statistical Analyses

Differences in proportions between the 2 groups at all time points were compared with the Fisher's exact test for 2×2 tables, and the χ^2-test for larger tables. The Pearson exact χ^2-method was used wherever small cell counts were a concern. Tests for trend were performed using the Cochran-Mantel-Haenszel test to compare trends over time within groups (biopsy vs normal PSA), and the Breslow-day test for homogeneity of odds ratios to examine whether the difference in proportions between the groups changed over the 3 time points. Ordinal logistic regression models were utilized to assess group effect at 6 and 12 months adjusting for potential confounding factors (history of BPH or prostatitis, number of previous PSA tests at 6 weeks, and number of previous visits to an urologist reported at 6 weeks).

RESULTS

Study Sample Characteristics

There were no significant differences between the groups in age, race/ethnicity, marital status, education, health status, or family history of prostate cancer (Table 1). Compared with the normal PSA group, more of the biopsy group had histories of benign prostatic hyperplasia and prostatitis, and they reported more previous PSA tests, and visits to urologists.

Psychological Impact

Compared with the normal PSA group, the biopsy group more often reported thinking and worrying about prostate cancer at every time point and more often reported thinking their chance of getting prostate cancer was greater than average. Figure 1 shows that 2 of the 3 measures drop significantly between 6 weeks following the biopsy and the 6-month follow-up, but hold steady or rise slightly between 6 and 12 months. The perception of elevated risk of cancer rose steadily throughout the year after the biopsy. At every point, these perceptions were significantly higher among the biopsy group than among the normal PSA group.

Socio-behavioral Impact

Data for the 12-month time point are presented in Table 2. Results at 6 months were essentially the same except for the proportion of men in the normal PSA group who read articles about prostate cancer, which went from 45% at 6 months to 56% at 12 months. The difference between the groups on this item was significant at 6 months (P=.01). The biopsy group reported more often having talked with their wife or significant other about prostate cancer and more often reported thinking their wife or significant other was concerned about them developing prostate cancer. More men in the biopsy group compared with the normal PSA group reported seeking information about prostate cancer on the Internet, and this group reported feeling more informed about prostate cancer.

Medical Care

Medical record review revealed that over 1-year of follow-up the biopsied men had more follow-up PSA tests and prostate biopsies than the normal PSA group, and the survey revealed they had more office visits and calls to urologists (Table 3). Thirty-three percent (40/121) of men in the biopsy group had 2 or more follow-up PSA tests; of these, 25 men had 2, 13 men had 3, and 2 men had 4 additional PSA tests within the year.

We stratified by history of BPH and prostatitis to see if the additional follow-up may have resulted from these other urological problems. Among men in the biopsy group, there were no differences with respect to history of BPH in the number of additional PSA tests, prostate biopsies, or visits to the urologist; however, more men in the biopsy group with a history of prostatitis had visited the urologist more than 2 times (56% vs 31%, P=.03). There were no differences according to prostatitis status within the biopsy group in number of additional PSA tests or prostate biopsies.

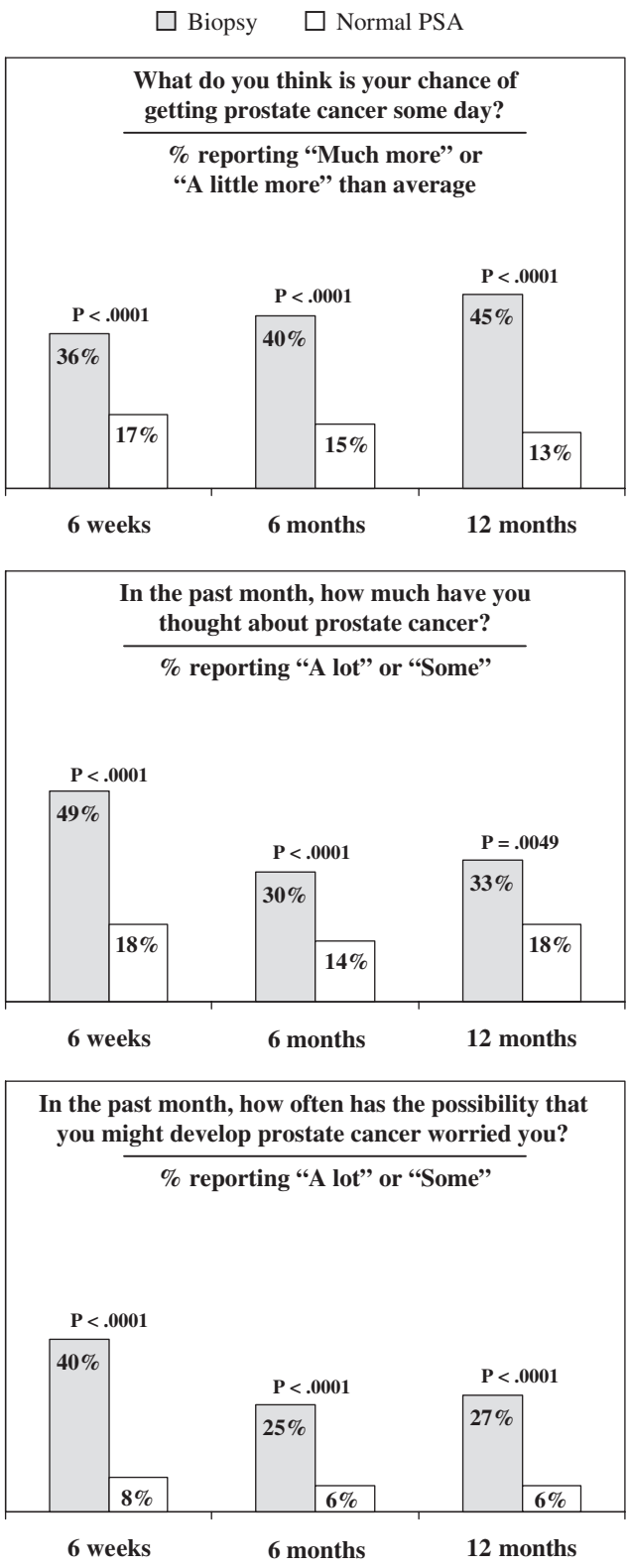

FIGURE 1. Psychological impact at 6 weeks, 6 months, and 12 months by group.

The vast majority of men (>90%) in both groups reported (at 1-year follow-up) planning to have regular PSA tests in the future, and that they would have a biopsy if their doctor recommended it.

DISCUSSION

We found that a considerable proportion of men with benign prostate biopsies after suspicious screening tests reported a negative psychological impact at 6 and 12 months, which extends our previous work showing a negative psychological impact at 6 weeks. Men with benign prostate biopsies reported substantial thinking and worrying about prostate cancer, even after the benign biopsy. In addition there appeared to be associated psychological, socio-behavioral, and medical utilization implications, demonstrating that the impact was an important one. Men in the biopsy group were more likely than men in the normal PSA group to report talking with their wife or significant other about prostate cancer, thinking their wife or significant other was worried about prostate cancer, searching on the Internet about prostate cancer, visiting the urologist, and undergoing additional PSA tests and prostate biopsies.

Investigators from the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial (PLCO), have described the medical and nonmedical costs associated with false-positive prostate cancer screens.[13] The PLCO trial found that men with false-positive prostate cancer screening results were nearly twice as likely not to return for further prostate cancer screening, compared with men with normal prostate cancers screening results.[14] Our survey contrasted with this finding; the vast majority of men in our study reported being committed to having subsequent screening tests. In fact, our medical record review showed fully 71% of men in the biopsy group had at least 1 more screening PSA test in the subsequent year. The differences in the findings between our study and the PLCO substudy may be related to study design; the PLCO study was a population based screening trial, whereas our study was a nonrandomized, comparative study that recruited men from primary care physician offices. Although our study population and methodology differed, our findings are consistent with those of Schwartz et al.,[15] who found that the public is enthusiastic about cancer screening, and the commitment is not dampened by false-positive test results. The finding that about 1-third of men in our biopsy group had between 2 and 4 additional PSA tests and 15% had another prostate biopsy within the year suggests that physicians and patients do not view the initial benign biopsy result as entirely reassuring, and physicians continue closely monitoring these men. It is noteworthy that the biopsied men were regular patients of urologists over the year of follow-up; 71% had seen an urologist at least once and 38% had 2 or more urology visits. This ongoing surveillance and the possibility of a false negative biopsy may help propagate the anxiety we documented among these men.

Concern about false-negative biopsy results is fairly unique to prostate cancer screening. In addition to lower specificity (therefore more false positives) than breast and colorectal cancer screening,[1,16,17] the follow-up test, transrectal ultrasound-guided biopsy, involves random sampling of the prostate gland (in addition to targeted biopsies of suspicious areas), causing mounting concerns about false-negative biopsies.[18] Whereas a benign biopsy in response to an abnormal mammogram is fairly reassuring (because the abnormal area of the breast has been visualized and biopsied), the elevated screening PSA, a blood test, simply represents a general indictment of the prostate gland, and, because of the poor negative predictive value of the random biopsy, at least 10% of

Table 2. Sociobehavioral Impact at 12 Months*

Item	Number (%)		*P* Value
	Biopsy Group *N*=121	Normal PSA Group *N*=164	
Currently married/significant other	*N*=101 (84)	*N*=134 (83)	*P*=.9
In the past month, how much have you talked with your wife or significant other about prostate cancer? (for those married/have significant other*)			
A lot	0 (0)	0 (0)	*P*=.001
Some	11 (11)	4 (3)	
Only a little	35 (35)	27 (21)	
Not at all	55 (54)	100 (76)	
How much do you think your wife or significant other is concerned about your developing prostate cancer? (for those married/have significant other*)			
A lot	9 (9)	4 (3)	*P*<.0001
Some	37 (37)	15 (11)	
Only a little	35 (35)	52 (39)	
Not at all	19 (19)	62 (47)	
In the past 6 months, have you read any books about prostate cancer?			
Yes	8 (7)	7 (4)	*P*=.43
No	112 (93)	154 (96)	
In the past 6 months, have you read any articles in magazines or the newspaper about prostate cancer?			
Yes	71 (59)	90 (56)	*P*=.63
No	49 (41)	71 (44)	
In the past 6 months, have you gone on the Internet for information about prostate cancer?			
Yes	16 (13)	6 (4)	*P*=.006
No	104 (87)	155 (96)	
How well informed do you feel about prostate cancer?			
Very well	19 (16)	16 (10)	*P*=.01
Fairly well	90 (76)	111 (69)	
Not well at all	10 (8)	33 (21)	

**Number for individual items vary slightly because of nonresponse.*
PSA, prostate-specific antigen.

Table 3. Medical Care at 12 Months*

Item	Number (%)		*P* value
	Biopsy Group *N*=121	Normal PSA Group *N*=164	
Number of times visited primary care physician over 12 months			
0 times	19 (16)	19 (12)	*P*=.6
1 time	35 (29)	49 (30)	
2 or more times	67 (55)	96 (58)	
Number of times called primary care physician over 12 months			
0 times	81 (67)	93 (57)	*P*=.1
1 time	21 (17)	30 (18)	
2 or more times	19 (16)	41 (25)	
Number of times visited urologist over 12 months			
0 times	35 (29)	142 (87)	*P*<.0001
1 time	40 (33)	10 (6)	
2 or more times	46 (38)	12 (7)	
Number of times called urologist over 12 months			
0 times	92 (76)	158 (96)	*P*<.0001
1 time	18 (15)	4 (2)	
2 or more times	11 (9)	2 (1)	
Number of PSA tests over 12 months			
0	32 (27)	93 (58)	*P*<.0001
1	46 (39)	66 (41)	
2 or more	40 (34)	2 (1)	
Number of biopsies over 12 months			
0	100 (85)	159 (99)	*P*<.0001
1 or 2	18 (15)	2 (1)	

**Number for individual items vary slightly because of nonresponse.*
PSA, prostate-specific antigen.

men with a benign biopsy result will have prostate cancer detected on a subsequent biopsy.[19] Therefore, urologists are urged to perform repeat sets of biopsies[20] in men who have suspicious screening tests and initially benign biopsies.

The clinical significance of an elusive prostate cancer detected subsequent to a series of benign prostate biopsies has been questioned.[21] Djavan and colleagues prospectively examined the biochemical and pathological features of cancer detected on biopsies 1, 2, 3, and 4, as well as the biopsy-related morbidity. The investigators found that prostate cancers detected on biopsies 1 and 2 were similar, but that cancers detected on biopsies 3 and 4 had lower grade, stage, and volume compared with biopsies 1 and 2; moreover, the third and fourth biopsies were associated with higher complication rates. When to stop the biopsy cascade that has started, especially for men with conditions known to elevate the PSA level, such as BPH and prostatitis, deserves more attention. This is important because many of these men will have false-positive screening results, which may have psychological and socio-behavioral consequences. While only 1 biopsied man in our study had more than 1 subsequent biopsy during the follow-up year, 25% of the biopsy group reported at the baseline survey having already had 3 or more sets of biopsies, suggesting that the strategy of repeated sets of biopsies is not uncommon.

Our study had a number of limitations. The absence of pre-screening data precluded the determination of whether men in the 2 groups had equivalent baseline psychological profiles. In addition, the 2 groups were not comparable at baseline with regard to history of benign prostatic hyperplasia, prostatitis, previous PSA tests, and previous visits to urologists. However, adjustment for these factors in logistic regression models predicting key outcomes from group membership did not change our findings. Also, men who had a previous prostate biopsy were excluded from the normal PSA group, but not from the biopsy group. However, when we restricted our analyses to include only those men in the biopsy group without a previous biopsy, the findings were essentially unchanged, except that with the reduced power from the restricted sample the difference between the groups responses to the question "In the past month, how much have you thought about prostate cancer?" lost significance at 12 months (P=.16). Another potential limitation involves missing data; however, as the amount of missing data was small and the magnitude of the differences between groups was large it is unlikely that missing data made a difference in the findings from our study. Also, we obtained information about worry on the part of the spouse or significant other from the patient, rather than directly from the spouse or significant other[22,23]; however, we believe the perception of the patient regarding worry on the part of their intimate partner is an important issue. We limited our study population to men with a primary care physician at 1 of the 3 participating institutions, anticipating that most of the men would be receiving their health care in that setting. However, men were not asked whether they had any PSA tests or prostate biopsies performed elsewhere, and, therefore, it is conceivable that the number of follow-up PSA tests and prostate biopsies that we obtained from our electronic medical record review at the 3 participating institutions is an underestimation. Lastly, the sample primarily included well-educated white men, and the results may not be generalizable to other racial and ethnic groups, and men with less education. We recommend verification of the results of this study in other samples, particularly African Americans, who are at higher risk for prostate cancer.

In conclusion, we found that even benign prostate biopsy results have psychological, socio-behavioral, and medical consequences. For many men, the benign biopsy result does not put the question of prostate cancer to rest; but rather, is associated with additional urology visits, PSA testing, and prostate biopsies, all of which have consequences for the patient and his family. We do not know the relative contribution of patient and urologist concern to the patterns observed, but it is certainly clear that men with benign biopsies receive more follow-up medical care than those with normal PSA results. These hidden tolls associated with screening should be considered in the discussion about the benefits and risks of prostate cancer screening, particularly in men with benign prostatic hyperplasia or prostatitis, who are at higher risk of false-positive screening results. Although it may be the path of greater resistance,[24] physicians will better serve patients by acknowledging that screening for prostate cancer, although an attractive option for many, is not the best option for all.[25]

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