Characteristics and Experiences of Patients with Localized Prostate Cancer Who Left an Active Surveillance Program

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Abstract

Background—Understanding the experiences of men leaving active surveillance programs is critical to making such programs viable for men with localized prostate cancer.

Objective—To generate hypotheses about the factors that influence patients' decisions to leave an active surveillance program.

Methods—Using data from the Johns Hopkins active surveillance cohort, bivariate analyses and multinomial regression models examined characteristics of men who self-elected to leave, those who stayed in the program, and those who left because of disease reclassification. We interviewed patients who self-elected to leave.

Results—Of 1,159 men in active surveillance, 9 % self-elected to leave. In interviews with a sample of 14 men who self-elected to leave, uncertainty involved in active surveillance

participation, existence of personal criteria— distinct from providers' clinical criteria—and fear of cancer were important factors in decisions to leave.

Conclusion—Men leaving active surveillance were motivated by a number of factors, including patient-defined criteria, which might differ from clinical recommendations. To ensure active surveillance participation, it may be important to address cancer-related anxiety and personal criteria underlying patient decisions.

1 Introduction

Overtreatment of localized prostate cancer is an important problem. Once diagnosed with prostate cancer, the majority of men undergo treatment with radical prostatectomy or radiation, regardless of their age or health status [1]. Treatment-related side effects in a significant proportion of men [2] may negatively impact the health-related quality of life of patients and partners [3–5].

Active surveillance may mitigate overtreatment for men with low-risk disease. However, for this to be true, men need to not only choose active surveillance but also remain in the program. The 2011 National Institutes of Health (NIH) State-of-the-Science Conference statement on the role of active surveillance in the management of men with localized prostate cancer called for additional research to understand men's experiences of active surveillance, specifically examining the reasons why men leave surveillance programs [6].

Between 3 and 18 % of men in active surveillance cohorts elect to leave active surveillance, without evidence of disease progression [7–10]. In this mixed-methods study, we first used administrative data to examine whether the characteristics of men who left active surveillance without evidence of disease progression were significantly different at baseline from those who remained in the program. We then performed semi-structured qualitative interviews with men who left the program without disease progression, to better understand their experiences in active surveillance and their reasons for withdrawing from the program. These were supplemented with interviews of men who left active surveillance because of disease reclassification, in order to contrast potential experiences and opinions. Such mixed-methods methodology is particularly suited to such an investigation of patients' experiences and has been frequently used in cancer outcomes research in general [11], as well as in studies of patient experience in localized prostate cancer in particular [12].

2 Methods

2.1 Cohort from the Johns Hopkins Active Surveillance Program

We evaluated patients in the prostate cancer active surveillance program, a prospective open-enrollment study at the Brady Urological Institute at Johns Hopkins School of Medicine (Baltimore, MD, USA). We began with a database of enrolled men who met criteria for very low-risk prostate cancer: clinical stage T1c, prostate-specific antigen (PSA) density <0.15 ng/mL, and appropriate prostate biopsy findings (Gleason score 6, two or fewer cores with cancer, and 50 % cancer involvement of any core) [7]. The comprehensive database of the active surveillance program has been maintained since 1995 and has been described in detail in the literature [7, 13]. We retrieved information since the

beginning of the program on men who had elected to leave active surveillance, men who had left active surveillance following a physician's recommendation, and men who remained in the active surveillance program as of 2013. For our qualitative interviews, we included men who left the program within the last 3 years (2010–2013); this timeframe was chosen in order to reduce recall bias. The study was approved by the Johns Hopkins Medicine Institutional Review Board.

2.2 Quantitative Data and Analysis

We examined characteristics on entry into the active surveillance program that might be associated with decisions to leave, including sociodemographic characteristics (age at diagnosis, race/ethnicity, educational status, and marital status), clinical characteristics (PSA level <4, 4 to<10, or 10 ng/mL), and family history of prostate cancer and of any cancer. We did not include the Gleason score, because 99 % of enrollees had a Gleason score of 6. We included in our quantitative analysis the subgroup of men who left following a physician's recommendation, to highlight by contrast the characteristics of the men who self-elected to leave.

We first examined unadjusted differences according to whether the patient was currently enrolled in active surveillance, left following a physician's recommendation, or self-elected to leave (using analysis of variance [ANOVA] for continuous variables and Fisher's exact test for categorical variables).

We then performed a multinomial regression model using all covariates, where our outcomes were currently in active surveillance (baseline), left following a physician's recommendation, and self-elected to leave. Such regression modeling has been used for a number of years to study outcomes in patients with prostate cancer. With such a technique, we set out to compare people who were recommended to leave active surveillance and people who stayed, controlling for relevant covariates, then we performed a similar comparison between men who self-elected to leave and those who stayed in the program [14].

Because not all men in the active surveillance cohort completed the intake survey, we used multiple imputations to account for missing data [15]. Missingness ranged from 20 % (for a family history of prostate cancer and a family history of other cancers) to less than 1 % (for race). We implemented chained imputations in STATA software, using the mi impute chained function, and modeled the resulting multinomial regression using mi estimate [16]. We performed a separate regression model as a sensitivity analysis, including the categories of men who withdrew from active surveillance at Johns Hopkins without receiving treatment, or were lost to follow-up.

2.3 Qualitative Data Collection and Analysis

After sending an introductory letter to men who had left active surveillance within the last 3 years, we invited men by telephone to participate in semi-structured interviews. We attempted to contact by telephone, at least once, every man in this group of those leaving active surveillance who had not explicitly opted out.

Our initial categories of questions included themes based on previous knowledge, including the circumstances of the patient's diagnosis, his experiences in active surveillance, and his decisions regarding leaving active surveillance (see the Electronic Supplemental Material). Our aim was to generate hypotheses about the factors that influenced patients' decisions to leave the active surveillance program. In the qualitative approach known as modified grounded theory, data collection and analysis each inform the other in an iterative process [17]. As we interviewed patients, the interview questions evolved to include themes that emerged from the interviews, including reasons for initial participation in active surveillance, the influence of loved ones' experiences, and the issue of cancer beliefs. As new themes arose in the interviews, interviewers explored these themes in later interviews in greater detail.

Interviews were digitally recorded and transcribed. We coded the transcriptions using thematic analysis; our methodology was informed by modified grounded theory, in which prior knowledge and empirical literature help identify which elements of patient experience are of greatest interest [18–20]. The first three interviews were carefully read by all co-investigators individually and as a group, using open coding, in which phrases, paragraphs, and exchanges were labeled. The labels were derived from the content of the transcripts, though emerging codes were informed by our knowledge of the subject area. Team meetings achieved consensus on the emerging codes. After this initial consensus, the codes were organized into larger categories. Further transcripts were read by all team members but were coded by one investigator (Z.B., C.P., or J.Y.), with a second coder reviewing the coding. Subsequent meetings led to further refinement and categorizations of the themes, with coding differences resolved by consensus. We conducted interviews until we achieved thematic saturation.

3 Results

3.1 Quantitative Analyses

A total of 1,159 patients have been enrolled in the active surveillance program since 1995. Table 1 presents the baseline characteristics of men who remained in the active surveillance program as of August 2013 ($n = 584$), those who left (were treated) because of disease reclassification ($n = 311$), and those who left (were treated) without evidence of disease reclassification ($n = 103$). The remaining 161 patients withdrew from the program without being treated ($n = 31$), are no longer in the Johns Hopkins program but are being followed elsewhere ($n = 69$), were lost to follow-up ($n = 15$), or are deceased ($n = 46$). The average length of time in active surveillance is 4.2 years (standard deviation [SD] 2.6) for those currently enrolled, 1.9 years (SD 1.7) for those who left following a physician's recommendation, and 1.7 years (SD 1.4) for those who self-elected to leave.

As shown in Table 1, there were significant differences across groups in the unadjusted analyses. Men who self-elected to leave active surveillance tended to be younger than those who remained in the program. Thirty-one percent of men still in active surveillance had a baseline PSA level <4 ng/mL, compared with 22 % of those who self--elected to leave the program. Though there were statistically significant differences between groups in the

percentages of men who had a family history of prostate cancer or of any cancer, the rate of missingness for these variables was high.

Table 1 presents the results of our multinomial logistic regression model, where the outcome categories were remaining in active surveillance (baseline), self-electing to leave active surveillance, and leaving following a physician's recommendation. Men older than 70 years at diagnosis were significantly less likely to self-elect to leave active surveillance than those aged between 40 and 60 years (relative risk ratio [RRR] 0.16, 95 % confidence interval [CI] 0.06–0.42). Men with PSA levels in the 4–10 ng/mL range were more likely to self-elect to leave (RRR 2.09, 95 % CI 1.13–3.85) or to leave following a physician's recommendation (RRR 1.79, 95 % CI 1.25–2.58) thanmen withPSA levels <4 ng/mL. No other variables were significant in the multinomial model with imputation; the results did not significantly change when imputation was not used (see Appendix Table 2) or in a sensitivity analysis including those men who withdrew from the program or were lost to follow-up (see Appendix Table 3).

3.2 Qualitative Analyses

Of the 35 men who left the program from January 2010 to August 2013, we conducted interviews with 14 men who elected to leave of their own accord. We further performed interviews with seven men who left following a physician's recommendation. In general, the themes found among those who left following a physician's recommendation did not differ from the themes among men who self-elected to leave active surveillance. We do not show the patient characteristics of the interviewed patients, because of the small sample sizes of these groups and resulting concerns about confidentiality.

3.3 Main Themes

We examined the reasons why patients initially chose to enter the active surveillance program, since these reasons might have framed subsequent decisions to leave active surveillance.

3.3.1 Reasons for Participating: "You've Got a 25-Year Outlook Before It's Going to Kill You"—Patients in the active surveillance program articulated several key factors in their initial decision to participate, such as a low statistical risk of death from prostate cancer and the fact that they could live several decades before any decision to actively intervene need be made. This observation was found among those self-electing to leave, as well as among those leaving following a physician's recommendation.

> When someone is saying, 'You've got a 20- to 25-year outlook before it's going to kill you,' and you're at that time—68, 69—statistically, it made sense. [Self-elected to leave active surveillance]

Some also noted the additional benefit of avoiding aggressive treatment for as long as possible.

3.3.2 Follow-Up in Active Surveillance: "Getting the Oil Changed"—Further, we examined the process of follow-up in active surveillance itself, which we reasoned might shed light on patients' experiences in the program and their resultant decisions to leave.

Some patients downplayed the stress or anxiety associated with undergoing an annual biopsy for prostate cancer, normalizing it as an inevitable part of active surveillance:

> It's just something you get fixed—need to get your oil changed. [Self-elected to leave active surveillance]

Some reported that regular monitoring was a source of relief and confidence, especially when provided by a provider they trusted.

> It wasn't—you know—an anxious time for me or anything like that. I felt confident that at any time I could change my mind. And so it wasn't really that difficult, I think. [Self-elected to leave active surveillance]

The reassurance provided by regular monitoring was also mentioned by patients who chose to leave active surveillance following a physician's recommendation.

3.3.3 Reasons for Seeking Treatment: "A Time to Do It"—Among the patients who left without disease progression, a common thread in their narratives was the existence of personal criteria—not always correlated with clinical criteria—for discontinuing active surveillance. These patients were willing to continue to participate in the monitoring that was offered, but they were not sure how long they could continue, especially if their cancer became more aggressive. For some men, the decision to seek treatment was seen as inevitable; active surveillance was a way to delay treatment rather than avoid it entirely.

> It was 7 years. I figured I was pushing my luck. I figured there was a time to do it, so I did it. Only, I did it closer to where I live. See, I was travelling 2 hours to the hospital, Johns Hopkins. I did that for 7 years. So I figured I got away with it for 7 years, but I didn't want to push my luck anymore. That was my basic reasoning. I thought it was time to make a move, so I did. [Self-elected to leave active surveillance]

Some patients left once the uncertainties of biopsy became intolerable:

> It wasn't like I was going crazy from thinking about it, but the thoughts were there … I knew just from my study and my research on my path—look, just because those biopsies are not showing the cancer cells and so forth, in all probability it's in there. It's just that the biopsies are not picking the heat up … it was in my mind, maybe not constantly, but it was there often enough—to the point where, you know what, enough is enough. [Self-elected to leave active surveillance]

The sentiment that "enough is enough," i.e., that the uncertainties of biopsy results, together with the worry generated by the presence of cancer, reached a point that leaving the program was preferable, was shared by a number of patients. They were eager to have their cancer treated before it progressed, and they were not convinced that the active surveillance program would prevent this outcome, perhaps because the interval biopsies might miss such

changes. Thus, while some patients entered active surveillance as a way to avoid treatment, others might have found this lack of active treatment intolerable after a time.

Some patients used the physician's reaction to their annual biopsy as a key criterion in their decision making. These patients resolved to pursue treatment at the first sign of equivocation, regardless of the physician's recommendation:

> I would always ask something like, 'Do you feel like this is something that needs to be done now or do I need to take care of this now?' and he usually said, 'No, I don't think so.' That to me was a pretty definitive statement … the last time, it was, 'Well the numbers have changed, and they're going up' … so, to me, it was not a rubber stamp of 'Yup, let's keep in the program,' and I promised myself that the first time I felt that I didn't get that rubber stamp, I'd do something about it. [Self-elected to leave active surveillance]

Though men who left the program because of a physician's recommendation shared the above sentiments about the uncertainty of biopsy, they also commented that pursuing treatment was something best done when they were younger and better able to tolerate the procedure.

> You watch and wait, but sooner or later, if you're going to have it done, do you want to wait until you're 90 before you do it—like my father did—or you want to do it when you're healthy enough to have it done? So that was probably the biggest factor, I think, in the decision. [Recommended to leave active surveillance]

3.3.4 Fear of Cancer: "The Word 'Cancer' Scares Me"—A total of six patients who self-elected to leave active surveillance described a fear of cancer, which trumped clinical indications for surveillance of low-risk prostate cancer:

> Well, I guess the word 'cancer' scares me. I had a good friend who died with prostate cancer, and he was fairly young. [Self-elected to leave active surveillance]

Patients leaving following a physician's recommendation also expressed this fear ("the only way to deal with cancer is to cut it out").

3.3.5 Loved Ones' Worry and Experiences: "Being There for the Kids"—The experiences of friends and family members with cancer—often not even prostate cancer—was factored into some men's decision making. In three instances, patients reported that they pursued treatment and left the active surveillance program in order to limit their loved ones' worry, or in reaction to the fear of cancer expressed by their family. For example, one patient described his reaction to his children's worry about his prostate cancer:

> But having children, and people telling me that, 'Hey, you need to be there for the kids,' that sort of thing, I kind of thought of it differently than I would've if I were single or without children, I'd say. The children were a strong consideration in the decision making. [Self-elected to leave active surveillance]

4 Discussion

The results of this study highlight the challenges that men continue to face when on active surveillance for localized prostate cancer, and may point to potential avenues to support men in the program. In our quantitative analyses, we observed that higher baseline PSA levels and younger age were significantly associated with decisions to leave the program. Our qualitative results suggested that men who elected to leave continued to feel anxious about their cancer and viewed active surveillance as a way to delay rather than avoid treatment entirely.

The results from the quantitative analysis are contextualized by our qualitative findings. The quantitative analysis suggested that older patients are less likely to leave the active surveillance program. In addition, and unexpectedly, those with PSA levels of 4–10 ng/mL (and not those with PSA levels >10 ng/mL) were more likely to leave. Our sample was not large enough to directly assess the difference in themes raised by older versus younger patients, or by patients with different baseline levels of PSA. Instead, it is possible that quantitative findings, if replicated, may help target interventions, with the qualitative analysis generating hypotheses about factors that may need to be addressed.

From the point of view of the patient, undergoing regular monitoring related to prostate cancer was associated with both positive and negative experiences. Monitoring can help men avoid unnecessary treatment, but on the other hand, it can increase worry. In some cases, it could be that patients' initial satisfaction with monitoring rather than treatment turned to dissatisfaction at the uncertainty of repeated biopsies. We can speculate that, at least in some cases, outside factors (such as provider ambiguity or family experiences) might have served as a "tipping point" to change their attitude to monitoring versus treatment.

This work is situated in an existing literature concerning patients' uncertainty while on active surveillance. In this study, as elsewhere, uncertainty played a significant part in the decision making of these patients and in their interpretation of their disease state [21]. Prior work has tended to focus on the uncertainty of the final outcome and the experience of biopsies [22] and the interplay between the level of anxiety and the availability of information [23]. By contrast, in the present study, there was little reported worry over the follow-up visits or biopsies themselves, which were generally well tolerated. Feelings of anxiety seemed less attributable to uncertainty over the final outcome—which to many of the men was a foregone conclusion—than the lack of clarity concerning the correct time to ultimately pursue treatment.

Upon entering the program, as our qualitative results indicate, a number of patients had already come to conclusions about what triggers would spur them to exit active surveillance and embark upon treatment. As part of this phenomenon, some patients appeared to understand prostate cancer, like other cancers, to be something that cannot be left in the body and must be removed, echoing previous work showing that cancer-related anxiety influences patients' responses to clinically insignificant changes in PSA levels [24, 25].

Fear of cancer and resultant expectations might also affect the attitudes of patients' families [26, 27], as exemplified in our study by patients whose treatment was encouraged by their

loved ones. Some patients who left the active surveillance program of their own accord may have done so out of worry on the part of their family or loved ones. We thus speculate that involving partners, spouses, families, and loved ones in counseling and decision making around localized prostate cancer might aid retention in the surveillance program, since families' worry appears to be a significant influence in patients' decision making.

Such influence of the concept of "cancer" on the expectations and preferences of patients may reinforce the recommendation of the NIH State-of-the-Science Conference on the treatment of localized prostate cancer: "Because of the very favorable prognosis of low-risk prostate cancer, modifying the anxiety-provoking term 'cancer' for this condition should be strongly considered" [6]. In particular, since the fear of cancer seems to affect not just patients' beliefs about proper treatment but also expectations about the proper duration of monitoring, as our interviews show, programs may consider ways to address this fear during active surveillance [27].

This study involved a number of limitations. Many of the participants appreciated the fact that this was a program at a tertiary care academic center with designated support systems and frequent contact, including newsletters. Thus, the current study may be considered a study of participants in a "best case" program. Second, these patients were relatively homogeneous demographically, and so our results cannot be generalized to the entire population of men diagnosed with prostate cancer on active surveillance. Third, this qualitative study set out to generate future directions for research and useful hypotheses, not to establish statistically significant results. Accordingly, the sample size was small. Fourth, we did not interview men who remained in the active surveillance program, whose experiences and beliefs may have been different than those of the men who left. Finally, we did not interview spouses or loved ones, who—as shown here—play a large role in patients' decision making. In spite of these limitations, the success of the program in recruiting and retaining participants makes it important to examine the reasons why these patients sought treatment.

5 Conclusion

We found that men older than 70 years and those with a PSA level between 4 and 10 ng/mL were more likely to leave the active surveillance program. Our qualitative analysis identified several types of experiences and beliefs that influenced patients' reasons to withdraw from the program. Common to many of them was patients' awareness of personal criteria, which might differ from diagnostic or professional criteria. Lack of complete reassurance on the part of the physician, a conviction (often based on family experiences) that cancer is something that should always be removed from the body, and the idea that there is a time when uncertainty about biopsy results becomes too much to bear were other factors that were discussed as having influenced decision making. To our knowledge, our study is the first to have specified these elements of patients' experiences and their possible relation to decision making. While previous studies have identified similar themes, ours is the first to have brought together these various elements, showing that possible interventions should focus not just on general anxiety or worry but possibly also on accompanying health beliefs.

Our results suggest several strategies—many of which overlap with the recommendations of the NIH State-of-the-Science Conference—to support men in active surveillance programs. As indicated by our quantitative results, focus may be directed toward younger men and men with higher baseline PSA levels. For some, as was indicated by patient interviews in this study, the word "cancer" may pose a barrier to remaining in active surveillance programs. Working with patients and families may also help retain men in active surveillance programs. Addressing uncertainty in the context of cancer anxiety and facilitating patients' coping with uncertainty around the timing of treatment may help expand the role of active surveillance in localized prostate cancer [28, 29].

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Appendix

See Tables 2 and 3.

Table 2

Multinomial model without imputation of missing variables, comparing men who remain in the active surveillance program, men who left the program on a clinician's recommendation, and men who self-elected to leave the program. Men with missing variables are excluded from the regression model[a,b]

	RRR (95 % CI)[c]	
	Left on physician's recommendation	Self-elected to leave
Age at diagnosis		
40 to <60 years	1 (reference)	1 (reference)
60 to <70 years	0.97 (0.60–1.57)	0.55 (0.30–1.02)
70 years	1.08 (0.63–1.85)	**0.16 (0.06–0.43)**
PSA level at diagnosis		
<4 ng/mL	1 (reference)	1 (reference)
4 to <10 ng/mL	**1.71 (1.17–2.48)**	**1.95 (1.09–3.50)**
10 ng/mL	0.80 (0.38–1.66)	0.74 (0.21–2.65)
Race/ethnicity		
White	1 (reference)	1 (reference)
Black	1.24 (0.64–2.42)	0.67 (0.19–2.37)
Other	1.28 (0.50–3.27)	0.43 (0.05–3.42)
Family history of prostate cancer		
No	1 (reference)	1 (reference)

	RRR (95 % CI)[c]	
	Left on physician's recommendation	Self-elected to leave
Yes	1.10 (0.75–1.62)	1.24 (0.69–2.21)
Family history of any cancer		
No	1 (reference)	1 (reference)
Yes	1.17 (0.83–1.65)	1.26 (0.74–2.15)
Education		
Less than college	1 (reference)	1 (reference)
Bachelor's degree	1.06 (0.65–1.73)	0.55 (0.26–1.14)
Graduate degree	0.82 (0.52–1.29)	0.64 (0.34–1.21)
Marital status		
Not married	1 (reference)	1 (reference)
Married or partnered	0.86 (0.53–1.38)	0.40 (0.15–1.03)

CI confidence interval, *RRR* relative risk ratio

[a] Excludes patients who withdrew from the program without being treated ($n = 31$), are no longer in the Johns Hopkins program but are being followed elsewhere ($n = 69$), were lost to follow-up ($n = 15$), or are deceased ($n = 46$)

[b] In the multinomial model, the reference category is men who remain in the active surveillance program. The models simultaneously adjust for all covariates listed in the table. Only completely ascertained cases are included in the regression model

[c] Bold text indicates significance at the $p < 0.05$ level

Table 3

Multinomial model comparing men who remain in the active surveillance program (baseline), men who withdrew from the program/were lost to follow-up, men who left the program on a physician's recommendation, and men self-elected to leave the program. Men with missing variables are excluded from the regression model[a,b]

	RRR (95 % CI)[c]		
	Withdrew/lost to follow-up ($n = 46$)	Left on physician's recommendation ($n = 311$)	Self-elected to leave ($n = 103$)
Age at diagnosis			
40 to <60 years	1 (reference)	1 (reference)	1 (reference)
60 to <70 years	0.93 (0.29–2.97)	0.97 (0.59–1.56)	0.55 (0.30–1.01)
70 years	0.89 (0.24–3.36)	1.08 (0.63–1.85)	**0.16 (0.06–0.43)**
PSA level at diagnosis			
<4 ng/mL	1 (reference)	1 (reference)	1 (reference)
4 to <10 ng/mL	1.11 (0.45–2.74)	**1.71 (1.17–2.48)**	**1.95 (1.09–3.49)**
10 ng/mL	1.05 (0.21–5.19)	0.79 (0.38–1.66)	0.74 (0.20–2.65)
Race/ethnicity			
White	1 (reference)	1 (reference)	1 (reference)
Black	Undefined	1.24 (0.64–2.41)	0.68 (0.19–2.40)
Other	Undefined	1.28 (0.50–3.28)	0.43 (0.05–3.45)
Family history of prostate cancer			

	RRR (95 % CI)[c]		
	Withdrew/lost to nbsp;follow-up ($n = 46$)	Left on physician's recommendation ($n = 311$)	Self-elected to leave ($n = 103$)
No	1 (reference)	1 (reference)	1 (reference)
Yes	0.65 (0.22–1.95)	1.11 (0.75–1.63)	1.23 (0.69–2.20)
Family history of any cancer			
No	1 (reference)	1 (reference)	1 (reference)
Yes	1.09 (0.47–2.52)	1.17 (0.83–1.64)	1.29 (0.75–2.20)
Education			
Less than college	1 (reference)	1 (reference)	1 (reference)
Bachelor's degree	0.59 (0.11–3.16)	1.07 (0.65–1.74)	0.55 (0.26–1.16)
Graduate degree	0.71 (0.11–3.33)	0.82 (0.52–1.29)	0.64 (0.34–1.20)
Marital status			
Not married	1 (reference)	1 (reference)	1 (reference)
Married or partnered	1.10 (0.37–3.34)	0.87 (0.54–1.40)	0.41 (0.16–1.06)

CI confidence interval, *RRR* relative risk ratio

[a]Excludes patients who are no longer in the Johns Hopkins program but are being followed elsewhere ($n = 69$) or are deceased ($n = 46$)

[b]In the multinomial model, the reference category is men who remain in the active surveillance program. The models simultaneously adjust for all covariates listed in the table. Only completely ascertained cases are included in the regression model

[c]Bold text indicates significance at the $p < 0.05$ level

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Key Points for Decision Makers

Patients with very low-risk prostate cancer may leave active surveillance prostate cancer programs, motivated by their own personal criteria for seeking treatment, which may differ from formal clinical or physician criteria.

These personal criteria might come to the fore in situations of cancer-related or decision-related anxiety.

Such anxiety should be addressed to improve patient participation in such programs.

Table 1

Descriptive statistics and multinomial model with imputation, comparing men who remain in the active surveillance program, men who left the program on a physician's recommendation, and men who self-elected to leave the program[a]

	Men [n (%)]			p value[b]	Multinomial model RRR (95 % CI)[c,d]	
	Currently in AS	Left on physician's recommendation	Self-elected to leave		Left on physician's recommendation	Self-elected to leave
N (%)	584 (100 %)	311 (100 %)	103 (100 %)			
Age at diagnosis (years)				0.006		
40 to <60	97 (17)	46 (15)	24 (23)		1 (reference)	1 (reference)
60 to <70	344 (59)	191 (61)	69 (67)		1.02 (0.63, 1.63)	0.55 (0.29, 1.04)
70	143 (24)	74 (24)	10 (10)		1.16 (0.69,1.94)	**0.16 (0.06,0.42)**
PSA at diagnosis (ng/mL)				<0.001		
<4	179 (31)	65 (21)	23 (22)		1 (reference)	1 (reference)
4 to <10	331 (57)	226 (73)	74 (72)		**1.79 (1.25, 2.58)**	**2.09 (1.13, 3.85)**
10	52 (9)	18 (5)	6 (6)		0.78 (0.38, 1.61)	0.76 (0.21, 2.73)
Unknown	22 (3)	2 (\1)	0			
Race/ethnicity				0.31		
White	523 (89)	271 (87)	97 (94)		1 (reference)	1 (reference)
Black	43 (7)	24 (8)	4 (4)		1.34 (0.72, 2.50)	0.65 (0.18, 2.36)
Other	17 (3)	14 (5)	2 (2)		1.26 (0.48, 3.29)	0.46 (0.06, 3.67)
Unknown	1 (<1)	2 (\1)	0 (0)			
Family history prostate cancer				<0.001		
No	389 (69)	163 (56)	54 (53)		1 (reference)	1 (reference)
Yes	117 (20)	51 (16)	19 (18)		1.09 (0.74, 1.61)	1.24 (0.70, 2.18)
Unknown	78 (11)	97 (28)	30 (28)			
Family history any cancer				<0.001		
No	200 (27)	77 (21)	24 (18)		1 (reference)	1 (reference)
Yes	319 (63)	147 (51)	50 (53)		1.2 (0.87, 1.67)	1.25 (0.73, 2.15)
Unknown	65 (10)	87 (28)	29 (28)			
Education				0.31		
Less than college	89 (15)	42 (36)	19 (19)		1 (reference)	1 (reference)
Bachelor's degree	148 (25)	70 (23)	17 (17)		1.02 (0.62, 1.68)	0.52 (0.24, 1.11)

| | Men [n (%)] | | | p value[b] | Multinomial model RRR (95 % CI)[c,d] | |
	Currently in AS	Left on physician's recommendation	Self-elected to leave		Left on physician's recommendation	Self-elected to leave
Graduate degree	285 (49)	111 (36)	38 (37)		0.85 (0.54, 1.34)	0.64 (0.33, 1.25)
Unknown	62 (11)	88 (28)	29 (28)			
Marital status				0.25		
Not married	79 (14)	29 (9)	6 (6)		1 (reference)	1 (reference)
Married or partnered	443 (76)	195 (63)	68 (66)		0.81 (0.51, 1.27)	0.53 (0.22, 1.32)
Unknown	82 (11)	87 (28)	29 (28)			

AS active surveillance, CI confidence interval, RRR relative risk ratio

[a] Excludes patients who withdrew from the program without being treated (n = 31), are no longer in the Johns Hopkins program but are being followed elsewhere (n = 69), were lost to follow-up (n = 15), or are deceased (n = 46)

[b] Fisher's exact test

[c] In the multinomial model, the reference category is men who remain in the active surveillance program. The models simultaneously adjust for all covariates listed in the table

[d] Bold text indicates significance at the p < 0.05 level