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Patterns of Clinical Response to PSA Elevation in American Indian/Alaska Native Men: A Multi-center Pilot Study

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Abstract

Objective—To assess clinical treatment patterns and response times among American Indian/Alaska Native men with a newly elevated PSA.

Methods—We retrospectively identified men ages 50–80 receiving care in one of three tribally-operated clinics in Northern Minnesota, one medical center in Alaska, and who had an incident PSA elevation (≥ 4 ng/ml) in a specified time period. A clinical response was considered timely if it was documented as occurring within 90 days of the incident PSA elevation.

Results—Among 82 AI/AN men identified from medical records with an incident PSA elevation, 49 (60%) received a timely clinical response, while 18 (22%) had no documented clinical response.

Conclusions—One in five AI/AN men in our study had no documented clinical action following an incident PSA elevation. Although a pilot study, these findings suggest the need to improve the documentation, notification, and care following an elevated PSA at clinics serving AI/AN men.

Keywords

American Indian; Alaska Native; prostate specific antigen; prostate cancer

Prostate cancer is one of the most commonly diagnosed malignancies among men in the United States,[1] with an estimated 241,800 incident cases and 28,000 deaths in 2012[2]—and no less so in patients of American Indian and Alaska Native (AI/AN) ancestry.[3–5] There is

marked regional variation in prostate cancer incidence and mortality, particularly in Northern Plains AI men.[4,6–8] According to the most recent estimates, the prostate cancer mortality rate in this population was 41.6 deaths per 100,000 compared with 29.1 per 100,000 for the general U.S. population.[9]

Despite this excess regional burden of disease in AI/AN men, the etiology of the disparity in prostate cancer outcomes remains poorly understood. Although the overall U.S. population has experienced a gradual reduction in prostate cancer mortality due, in part, to the increased utilization of prostate specific antigen (PSA) testing as a primary screening tool,[10] and diagnosis of incident prostate cancer at earlier stages in the natural history of the disease,[11,12] the same trends have not been observed among AI/AN populations.[3,4] Patterns of care prior to and following an elevated incident PSA level and/or diagnosis of prostate cancer remain largely unknown in the AI/AN population.

Timeliness of follow-up care after an elevated PSA level may contribute to prostate cancer outcomes in AI/AN men. Delayed follow-up for an elevated PSA may also explain the disparity in advanced stage and metastatic prostate cancer incidence along with worse outcomes in other genitourinary conditions.[13] Delayed clinical responses for elevated PSA levels have been documented in the Veterans Affairs (VA) system.[14]

Borrowing principles from community-based participatory research,[15] we sought to determine the proportion of AI/AN men with an incident elevated PSA level who failed to get a timely clinical response, describe the spectrum of clinical responses to those PSA levels, and identify patient characteristics associated with a delayed or absent clinical response.

Methods

This study was approved by the Mayo Clinic Institutional Review Board (IRB) (IRB # 08-007402), the National Indian Health Service (IHS) IRB, and the IRBs and/or tribal councils of all collaborating sites.

Target population and local conditions

Participants at each of our three partnering sites in Northern Minnesota were enrolled members of a federally-recognized tribe seen at an on-reservation facility, while participants in Alaska resided in a geographically defined region surrounding a medical center which provides comprehensive medical services for AI/AN people living in Alaska. Most referral and specialty care at three of the four sites is conducted as *contract health*—that is, care that is provided by off-site specialists under contract with the IHS. The fourth site provides most of the necessary specialty care on-site.

We reviewed medical records from men who were 1) receiving or had ever received care at one of the four participating sites; 2) between the ages of 50 and 80 years (inclusive) at the time of the medical record search; and 3) had a documented PSA test result greater than or equal to 4.0 ng/ml[16–18] in laboratory databases. We further limited our cohort to those men

whose PSA elevation was incident (i.e., no documented evidence of prior elevations) and occurred between January 1, 2006, and May 31, 2009.

Two of our four participating sites use the IHS's electronic medical record (the Resource and Patient Management System, or RPMS), one uses a laboratory soft ware application to supplement RPMS, and one uses an alternate soft ware application. At each site, all available electronic medical record databases were searched using our eligibility criteria.

Data collection

We followed a similar methodological approach to that of Nepple *et al*,[13] in which the medical records of 327 men receiving care in a VA health care system were retrospectively reviewed for evidence of clinical response to newly elevated PSA results and the timeliness of those responses. Our team of two to three trained medical record abstractors manually collected basic demographics, insurance status, veteran status, and patterns of care using a standard chart abstraction instrument. Gathered variables included the timing, frequency, and nature of medical appointments following the elevated PSA test (i.e., records of both in-house and outside referrals), modes of communication between patient and provider (where present), the presence of co-morbidities (only those used in Charlson index[19] calculations, a 10-year prediction of mortality based on known comorbid conditions), and treatments and/or medications prescribed in response to the PSA elevation. We also ascertained the primary indication for performing the PSA test: 1) screening test for prostate cancer; 2) lower urinary symptoms; or 3) use within the context of prevalent benign prostatic hyperplasia (BPH) or acute prostatitis. All data were double-entered into a Microsoft Access database. Any discrepancies between information recorded by the data abstractors were clarified from the medical record.

Outcomes of interest

We defined a *clinical response* as an action documented in the medical record that was made in response to the incident PSA elevation, including further diagnostic testing, imaging, referral to a specialist (including appointments that were kept and those that were not), patient notification *via* phone call or letter, and/or empiric antibiotic therapy that was plausibly related to PSA elevation and genitourinary care. A clinical response was considered timely if it occurred within 90 days from the first abnormal PSA test, and delayed if it occurred more than 90 days from the incident PSA elevation. We reviewed medical records at least one year after each PSA elevation to ensure adequate ascertainment of initial follow-up care.

Statistical analysis

All data were analyzed using SAS version 9.1 (Cary, NC). We used basic descriptive statistics to examine frequencies and distributions of variables. We also used Pearson chi-square tests (or Fisher's Exact tests where cell counts were less than five) to assess associations between patient characteristics and timeliness of care. All statistical tests were two-tailed and assumed a significance level of $p \leq .05$ unless otherwise stated. We dichotomized participating sites into two regions: Northern Minnesota and a geographically defined region in Alaska.

Results

Eighty-two men were determined to be eligible (Table 1). The median age was 65 years (range: 50–80 years), one fifth were veterans (21%), the majority had smoked at some point in life (77%), and 5% had a family history of prostate cancer. The median incident elevated PSA level was 5.2 ng/ml (mean: 8.4 ng/ml; range: 4.0–121.2 ng/ml).

In our sample, the most common indication for PSA testing was prostate cancer screening (85%), followed by presumed BPH (9%) and acute prostatitis (6%). We observed no significant differences in demographic and clinical characteristics when comparing men from Northern Minnesota to those in Alaska (Table 1).

Six participants (7%) were diagnosed with prostate cancer following their incident elevated PSA. Of these, four had incident PSA levels ranging from 4.0 to 8.2 ng/ml and two had levels greater than 20 ng/ml. Four received a clinical response within 30 days of their incident PSA elevation (including one with an incident elevated PSA of 121.2 ng/ml), one within 90 days, and one 245 days after the incident elevation. For the latter patient, his incident PSA concentration was 4.0 ng/ml.

Among those with a documented clinical response to the incident elevated PSA (n = 64), the most common was specialty referral (51%), followed by a PSA re-test (25%), prescription of antibiotics (10%), a phone call or letter to the patient with test results (6%), a digital rectal exam (5%), and empiric treatment for BPH (3%). Two in five men (41%) received follow-up care within 30 days of incident PSA elevation, one in five (18%) received care between 31 and 90 days of the new elevation, one in five (18%) received care more than 90 days after the new elevation, and 22% had no follow-up care documented in the medical records (Figure 1).

Characteristics of men whose follow-up care was timely, delayed, or non-existent did not differ significantly (Table 2). We could find no evidence of a clinical response in the medical records of 15 of 54 men (28%) from the Alaska region, and three of 28 men (11%) from Northern Minnesota. The median index PSA value for these 18 men was 4.9 ng/ml (range: 4.0 to 7.5 ng/ml), while for the 64 men who received a clinical response of any sort (regardless of its timeliness) the median index PSA value was 5.4 ng/ml (range: 4.0 to 121.2 ng/ml). We did not have sufficient power to detect differences in follow-up time based on PSA levels or type of clinical response.

Discussion

In this pilot study, one in five AI/AN men (22%) had no documented clinical response following an elevated PSA test result, another one in five had a delayed response (over 90 days), and most (60%) had a documented clinical response within 90 days.

One VA-based study reported that the majority (77%) of men with an elevated PSA had a documented clinical response within 30 days, while 8% had a clinical response greater than a year following the abnormal PSA result.[13] In another VA cohort, Zeliadt *et al.* observed that 13% of men with an abnormal PSA did not receive appropriate follow-up within two

years of the elevated test.[14] Although our study used different sampling strategies and sizes and definitions of outcome variables (i.e., timeliness) preventing the ability to make direct comparisons, our findings are nevertheless consistent with these previous studies.

Furthermore, the disproportionate impact of prostate cancer mortality in Northern Plains American Indians and Alaska people in Alaska as documented by Cobb *et al.*[9] make delays similar to those found in the VA system all the more striking.

On a regional basis, prostate cancer mortality is significantly higher in the Northern Plains relative to Alaska. However, suspected sub-regional differences both in the Northern Plains and in Alaska may defy these generalizations. For instance, Minnesota's prostate cancer mortality rate for AIs based on CDC registry data are only slightly higher than the non-Hispanic white population,[20] and unpublished reports and clinical experience from Alaska suggest similar subregional variation. Despite these regional differences, there are no population-specific prostate cancer screening guidelines for AI/AN men that account for race/ethnicity or subregional differences. Furthermore, no national guidelines define what a timely response should be.

Limitations

Our approach relied on medical record review. Data abstractors frequently encountered gaps in patients' medical records and had to piece together information relevant to men's prostate care. Further, PSA tests conducted at other clinics but not recorded in records we reviewed would not have been ascertained. Finally, PSA tests were conducted at different reference laboratories; differences in assay methodologies with slightly different reference ranges may have influenced our ability to ascertain all eligible records. We also found that referral, diagnostic, and imaging records were frequently incomplete. References to a completed urology appointment did not consistently correspond to having a referral summary in the medical record.

Our definition of *clinical response* may have either omitted instances of appropriate but undocumented clinical responses, or been overly liberal by including a wide range of actions (including patient notification). However, our primary objective was to document the timeliness of a response—any response—to an incident PSA elevation. We determined that a broad interpretation of *clinical response* was best to meet this objective because it gives the benefit of the doubt to providers who may be providing timely follow-up care but whose documentation is sparse. To the extent that most incident PSA elevations should be referred for specialist evaluation, these numbers may represent a conservative estimate of the percentage of men who did not receive timely follow-up care.

Each of our participating sites faces its own unique set of challenges in communicating with patients, many of whom may have their own competing priorities (e.g., seasonal subsistence fishing activities, family responsibilities, and/or other illnesses) or who may not maintain current contact information. For example, while our collaborating site in Alaska provides comprehensive specialty care to its patients, its capacity to provide timely follow-up may be complicated by a patient's need to secure adequate food stores during the fishing and hunting seasons. This level of detail describing the reasons for the lack of timely follow-up

care cannot be ascertained from the medical record alone. In addition, it is possible that differences in the referral care structure among the health systems could have contributed to the differences in clinical care response times.

Clinical implications

The lack of a documented timely clinical response to elevated PSA concentrations, as well as inconsistencies in medical records (e.g., missing pathology reports, no notes from specialty appointments) suggest the need for improvements not only to the quantity and quality of clinical responses to elevated PSA among AI/AN men, but also in record keeping. Such improvements could draw upon resources of dedicated patient navigators as well as electronic tracking systems. Although patient navigators are most oft en used in coordinating cancer treatment in the post-diagnosis setting,[21,22] they could plausibly help patients through the steps following an abnormal cancer screening test. Recent upgrades in electronic medical records used at participating sites as well as emerging trends in patient portal technology may also create opportunities (and additional challenges) for more robust decision support systems to improve timely patient notification of incident PSA elevations.

Although recent guidelines call into question the utility of routine screening for prostate cancer in asymptomatic men,[23] whether to perform routine screening in AI/AN men introduces additional complexities. Many AI/AN men live in areas where specialty referral can involve significant geographic and logistical barriers that increase their likelihood of not having the necessary follow-up in place to clarify whether further tests or treatments are warranted. Having at least rudimentary follow up either in the form of repeat testing, empiric therapy for prostatitis or referral to a urologist are all clinical responses consistent with emerging guidelines.[24]

Conclusions

This study ascertained the timeliness of clinical responses to an elevated incident PSA and described some salient features of that care to the extent possible in a small pilot study. Approximately one in five AI/AN men in our study had no documented clinical response to their newly elevated PSA concentration (i.e., ≥ 4.0 ng/ml). That we observed delays in care following an elevated PSA test result, as well as a lack of clinical documentation in two different care settings (i.e., one with comprehensive specialty care—Alaska—and one with primary care alone—Minnesota) suggests the need for improved documentation, notification, and care in both types of settings. Addressing delays in clinical responses among AI/AN men with a newly elevated PSA will require a comprehensive approach adapted to the unique features of the care delivery context.

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Notes

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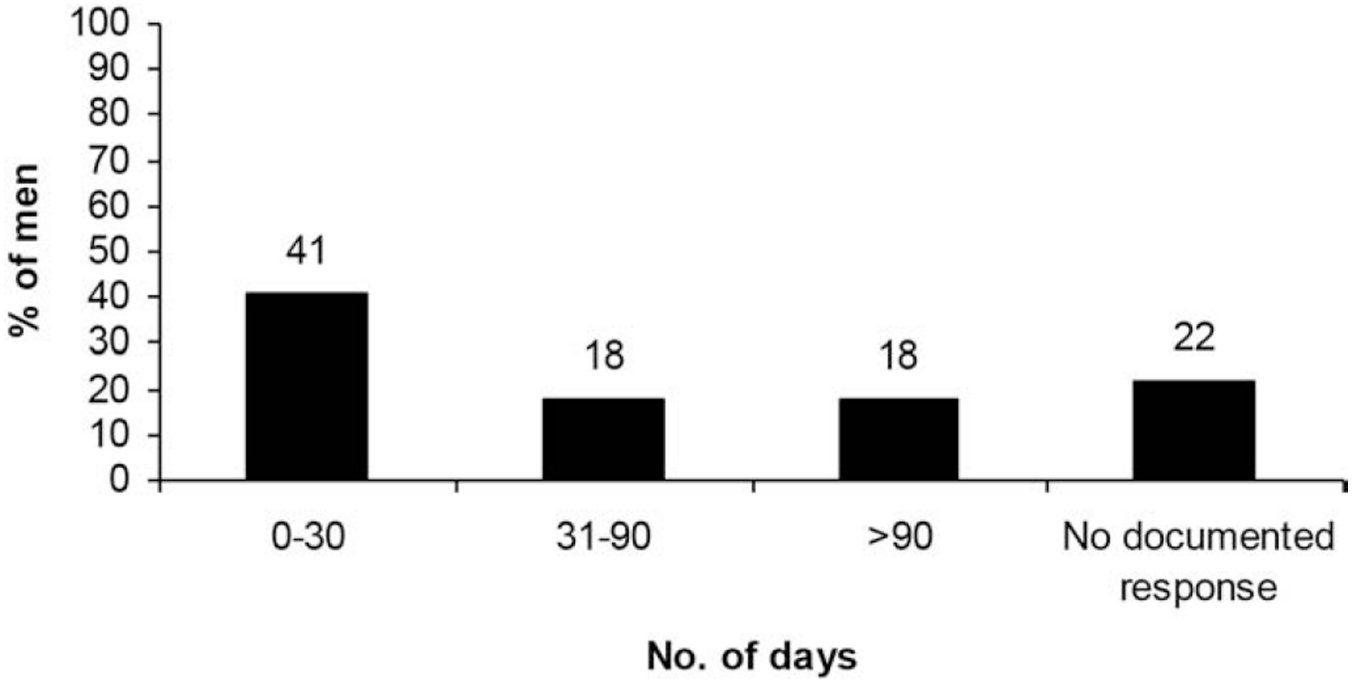

FIGURE 1.
Distribution of the number of days between incident elevated PSA levels and the first documented clinical response for 82 AI/AN men.

Table 1

Demographics and Clinical Characteristics of 82 AI/AN Men Who, Between January 1, 2006 and May 31, 2009, had a Newly Elevated PSA ≥ 4.0 ng/ml.

Characteristics & Features of Care	N (%)[a]
Age (years)[b]	
50–59	20 (26)
60–69	32 (42)
70–80	25 (32)
Insurance	
Medicare	21 (26)
Medicaid	12 (15)
Private	13 (16)
Other	19 (23)
Some combination of above	17 (21)
Veteran	17 (21)
Ever smoked	63 (77)
Family history of prostate cancer	4 (5)
Incident PSA value (ng/ml)	
4–10	76 (93)
≥ 11	6 (7)
No. co-morbidities[c]	
0	29 (35)
1–2	39 (48)
3+	14 (17)
Indication for PSA test	
Screening	70 (85)
Benign Prostatic Hypertrophy (BPH)	7 (9)
Acute prostatitis	5 (6)
Incident prostate cancer	6 (7)
Initial follow-up to PSA elevation[d]	
Referral to specialist	32 (51)
PSA re-test	16 (25)
Antibiotics	6 (10)
Phone call or letter to patient	4 (6)
Digital Rectal Exam	3 (5)
Empiric BPH treatment	2 (3)

[a] Numbers in each column may not total the overall N due to missing data.

[b] Age at time of medical record data extraction.

[c] As included in calculation of Charlson index (AIDS, cancer, cerebrovascular disease, chronic pulmonary disease, congestive heart failure, dementia, Type II diabetes, Type II diabetes with complications, liver disease, metastatic solid tumor, myocardial infarction, paralysis, peptic ulcer disease, peripheral vascular disease, renal disease, rheumatologic disease).

[d] A primary PSA follow-up action could not be ascertained for 18 of the 82 men (22%).

BPH = Benign Prostatic Hypertrophy

AI/AN=American Indian/Alaskan Native; PSA=Prostate specific antigen

Table 2

Time to Clinical Response to Incident Elevated PSA (≥ 4.0 ng/ml) by Demographic and Clinical Features of 82 AI/AN Men.

	N (column %)		
Characteristics and Features of Care	**Timely (≤ 90 days) (N = 49)[a]**	**Delayed or no documented response (>90 days or no response) (N = 33)**	**Chi-square p-value[b]**
Age (years)[c]			0.33
50–59	11 (25)	9 (29)	
60–69	16 (36)	15 (48)	
70–80	17 (39)	7 (23)	
Insurance			0.30
Medicare	16 (33)	5 (15)	
Medicaid	7 (14)	5 (15)	
Private	5 (10)	8 (24)	
Other	11 (22)	8 (24)	
Some combination of above	10 (20)	7 (21)	
Veteran	10 (20)	7 (21)	0.93
Region			0.28
Alaska	30 (61)	24 (73)	
Northern Minnesota	19 (39)	9 (27)	
Ever smoked	40 (82)	23 (70)	0.21
Family history of prostate cancer	2 (4)	2 (6)	0.36
Incident PSA value (ng/ml)			0.08
4–10	43 (88)	33 (100)	
≥ 11	6 (12)	0 (0)	
No. co-morbidities[d]			0.66
0	17 (35)	12 (36)	
1–2	22 (45)	17 (52)	
3+	10 (20)	4 (12)	
Indication for PSA test			0.80
Screening	41 (84)	29 (88)	
Benign Prostatic Hypertrophy (BPH)	4 (8)	3 (9)	
Acute Prostatitis	4 (8)	1 (3)	
Incident prostate cancer	5 (10)	1 (3)	0.18
Initial follow-up to PSA[e]			0.41
Referral to specialist	26 (54)	6 (40)	
PSA re-test	10 (21)	6 (40)	
Antibiotics	5 (10)	1 (7)	
Phone call or letter to patient	4 (8)	0 (0)	
Digital Rectal Exam	2 (4)	1 (7)	

Characteristics and Features of Care	N (column %) Timely (≤ 90 days) (N = 49)[a]	Delayed or no documented response (>90 days or no response) (N = 33)	Chi-square p-value[b]
Empiric BPH treatment	1 (2)	1 (7)	

[a] Numbers in each column may not total the overall N due to missing data.

[b] Or Fisher's exact test p-value where cell counts < 5.

[c] Age at time of medical record data extraction.

[d] As included in calculation of Charlson index (AIDS, cancer, cerebrovascular disease, chronic pulmonary disease, congestive heart failure, dementia, Type II diabetes, Type II diabetes with complications, liver disease, metastatic solid tumor, myocardial infarction, paralysis, peptic ulcer disease, peripheral vascular disease, renal disease, rheumatologic disease).

[e] A primary PSA follow-up action could not be ascertained for 18 of the 82 men (22%).