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Racial Differences in Longitudinal Changes in Serum Prostate-Specific Antigen Levels: The Olmsted County Study and The Flint Men's Health Study

Aruna V. Sarma, Ph.D.^a, Jennifer L. St. Sauver, Ph.D.^b, Debra J. Jacobson, M.S.^c, Michaela E. McGree, B.S.^c, George G. Klee, M.D., Ph.D.^d, Michael M. Lieber, M.D.^e, Cynthia J. Girman, Dr.P.H.^f, John M. Hollingsworth, M.D., M.S.^a, Steven J. Jacobsen, M.D., Ph.D.^g, and the Urologic Diseases in America Project

^aDepartment of Urology, University of Michigan, Ann Arbor, MI 48105

^bDivision of Epidemiology, Mayo Clinic College of Medicine, Rochester, MN 55905

^cDivision of Biomedical Statistics and Informatics, Mayo Clinic College of Medicine, Rochester, MN 55905

^dDepartment of Laboratory Medicine and Pathology, Mayo Clinic College of Medicine, Rochester, MN 55905

^eDepartment of Urology, Mayo Clinic College of Medicine, Rochester, MN 55905

^fMerck Research Laboratories, Blue Bell, PA 19422

^gDepartment of Research and Evaluation, Kaiser Permanente, Southern California, Pasadena, CA 91101

Abstract

Objective—To determine the distribution of and racial differences in changes in PSA from a population-based sample of men.

Materials and Methods—Data from two prospective cohort studies of a random sample of Caucasian men, ages 40–79 in 1990, followed biennially through 2007 and African-American men, ages 40–79 in 1996, followed through 2000 were examined to assess longitudinal changes in PSA concentrations. Serum PSA levels were determined at each examination for both cohorts and observations after a diagnosis of prostate cancer or treatment for benign prostatic hyperplasia (BPH) were censored. Observed and estimated annual percentage change in serum PSA levels were examined by race.

Results—At baseline, the median PSA level in Caucasian men did not differ from the median level observed in African-American men (Caucasian men: 0.9 ng/mL; African-American men: 0.9 ng/mL; P value=0.48). However, African-American men had a much more rapid increase in PSA level over time compared to Caucasian men (median annual percent change in PSA Caucasian men: 3.6%/year; African-American men: 7.9%/year; P value<0.001).

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Address for correspondence and reprint requests: Dr. Aruna V. Sarma, Department of Urology, University of Michigan, 2800 Plymouth Road, Building 520, Room 3171, Ann Arbor, MI 48109, office (734) 763-7514, fax (734) 232-2400, asarma@umich.edu.

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Conclusion—These data suggest that African-American men have more rapid rates of change in PSA levels over time. If the difference in rate of changes between African-American and Caucasian men is an early indicator of future prostate cancer diagnosis, earlier detection in African-American men could help to alleviate the racial disparities in prostate cancer diagnosis and mortality.

Keywords

Prostate cancer; PSA; racial differences; epidemiology

INTRODUCTION

Prostate cancer is the most common non-cutaneous cancer in U.S. men, with an estimated 217,730 new cases diagnosed in 2010¹. The age-adjusted incidence rate of prostate cancer in African-American men is 1.6 times higher than in Caucasian men translating into the highest incidence of prostate cancer in the world. Racial disparities in the age-adjusted incidence of prostate cancer diagnosis (231.9/100,000 vs. 146.3/100,000), and mortality (56.3/100,000 vs. 23.6/100,000)¹ between African-American and Caucasian men remain public health problems in the U.S. The cause of these racial differences remains unknown; however, hormonal, nutritional, genetic, and socioeconomic factors have been hypothesized as potential culprits².

The measurement of serum prostate-specific antigen (PSA) levels for the prediction of prostate cancer is one of the most widely used cancer screening tools. Earlier studies suggested that African-American men present with higher serum levels at initial diagnosis of cancer compared to Caucasian men and that these differences in PSA concentrations were responsible for racial disparity in cancer occurrence and outcomes^{3,4}. These studies, however, were limited by small sample sizes, lack adjustment for age or socioeconomic status, and consisted of selected clinical populations. Subsequent studies using population-based data were unable to support earlier reports of racial differences in PSA concentrations.

Prostate-specific antigen level is also elevated by a number of benign conditions. Because of this lack of specificity to prostate cancer, several investigators have explored using the change in serum PSA levels as an indication of prostate cancer⁵⁻⁸. Many of these studies have been conducted in select populations, primarily representing Caucasian men. These studies have noted that the change in serum PSA level over time depends on the starting PSA level^{8,9} and the interval between PSA measurements¹⁰; however, few have compared longitudinal changes in serum PSA levels by race⁹. McGreevy, et al. found a quadratic effect of age on PSA values over time in African-American men, but a linear effect of age on PSA values in Caucasian men in men undergoing annual screening for prostate cancer⁹.

In order to describe longitudinal changes in serum PSA measurements and compare these across race, we used information from two population-based cohorts: The Olmsted County Study of Urinary Symptoms and Health Status among Men (OCS; Caucasian men), and the Flint Men's Health Study (FMHS; African-American men).

METHODS

Study Subjects

Details on subject selection for both the OCS and FMHS have been previously published.^{11,12} Briefly, the OCS and FMHS are population-based, prospective cohort studies established to evaluate the natural history of urologic disease in Caucasian and African-American male residents of Olmsted County, Minnesota and Genesee County, Michigan,

respectively. In the OCS, 2,115 of 3,874 eligible Caucasian men aged 40–79 years in 1990 without history of prostatectomy, prostate cancer or specific conditions known to interfere with voiding function, completed the study protocol. From this cohort, a random sample of 537 men was selected for a detailed urologic examination that included a serum PSA determination, a digital rectal examination, uroflowmetry and transrectal ultrasound to estimate prostate volume and 476 (89%) participated. Further information on this cohort is available in a previous publication¹³. Using the same criteria and protocol described above, 730 of 943 eligible African-American men completed an interview-administered questionnaire in 1996 in the FMHS. Of these, 369 men underwent the comprehensive urologic examination, which included, as in the OCS, uroflowmetry, transrectal ultrasound, and serum PSA measurement and were deemed to be free of prostate cancer.

Follow-up

In the OCS, subjects were followed biennially through 2007, for a median of 7.5 years (25th, 75th percentiles: 3.3, 13.4). In the second and third biennial examination, men who dropped out of the study were replaced with men randomly chosen from the Olmsted County population (n=158 in the clinic subset). Observations after prostate or bladder cancer diagnosis or benign prostatic hyperplasia (BPH) treatment were censored leaving 616 OCS men for the current analysis. In the FMHS, four years after baseline in 2000, the 369 men who participated in the baseline clinical exam were re-contacted and invited to complete the same study protocol described above at follow-up. Of the 369 men, 175 (47%) completed the follow-up protocol. After censoring observations for prostate or bladder cancer diagnosis and BPH treatment, 150 men remain in the current analysis.

Measurements

Total serum PSA was measured in the exam phase in both the FMHS and OCS at each round using serum samples obtained prior to any prostatic manipulations, including digital rectal examination and transrectal ultrasound. In the FMHS, total serum PSA was determined using the Abbott AxSYM polyclonal-monoclonal immunoassay (Abbott Diagnostics, Abbott Park, IL), which had a lower limit of detection of 0.1 ng/mL. All total serum PSA levels for the OCS study were measured in the Mayo Immunochemical Research Core Laboratory. Over the course of the OCS three different PSA assays were used according to their individual manufacturer specifications. The different assays were found to be comparable with slightly, but non-significantly, higher results for the Tandem-E PSA assay at the levels measured in these cohorts. Samples from the first, fifth and sixth rounds of the OCS were tested with the Tandem-R monoclonal chemi-radiometric PSA assay (Hybritech Incorporated San Diego, CA). Samples were tested using the Abbott IMx assay (Abbott Diagnostics, Abbott Park, IL) in the second and third biennial rounds. Samples were tested with the Tandem-E PSA assay (Hybritech, Incorporated, San Diego, CA) in the fourth and final rounds. For the Mayo Immunochemical Research Core Laboratory, the coefficient of variation averaged 3–4% during this time period.

Statistical Analyses

Median, 25th and 75th percentiles of baseline total serum PSA levels were calculated on the basis of the empirical distribution of the data by age and race. Differences in baseline PSA levels by race were tested using the Kruskal-Wallis test. Linear mixed-effects regression models were used to estimate and test for differences in annual longitudinal changes in serum PSA level by regressing each measure on the time from initial serum PSA measurement, 10-year age groups and study. Interaction terms were included to allow for different slopes across age groups and study. An overall annual change for each man was determined by combining the average longitudinal changes (fixed effects) with the individual changes (random effects).^{14,15} Additional mixed models which included baseline

prostate volume and BMI measurements were used to adjust for prostate volume and BMI. The distributions of these changes were tabulated overall and stratified by age. Because serum PSA levels follow a log-normal distribution, regression analyses were based on natural log transformed serum PSA levels.

As the annual percent change in PSA levels was much greater for the African-American men and there were only two waves of measurement, we wanted to assess whether unknown changes may have led to changes in PSA levels over time independent of biologic factors. To determine whether unidentified changes had occurred, serum PSA measurements for each FMHS wave were assessed for their relationship with age and compared from wave 1 to wave 2. This process represents a practical way to assess and, if necessary, standardize data from samples collected and/or assayed at multiple points in time.

The OCS study was reviewed and approved by the Institutional Review Boards of the Mayo Clinic and Olmsted Medical Center. The FMHS study was reviewed and approved by the University of Michigan Institutional Review Board.

RESULTS

In Table 1, median baseline PSA levels in the cohorts are presented. The baseline serum PSA levels shown for the OCS cohort were largely those used in the development of the age-specific reference ranges¹⁶ but include men added as replacements in follow-up. The baseline levels shown for the subset of the FMHS cohort with follow-up are similar to those reported for the full FMHS cohort¹⁷. Overall, baseline PSA levels did not differ by race. Baseline PSA levels for older men were slightly lower among African-Americans; however, the differences were not significant.

In Table 2, annual percent changes in serum PSA level for the OCS and FMHS cohorts are presented. The overall annual percent changes in serum PSA level were approximately twice as high in African-American men compared to Caucasian men ($p=0.0005$). Age group differences were also approximately twice as high in African-American men compared to Caucasian men, with some indication that the difference in slopes for the two studies varied by age group ($p=0.24$). These differences remained after adjustment for prostate volume and body mass index and results were similar when the annual percent change in serum PSA level in the FMHS was calculated empirically (data not shown).

PSA levels across age were plotted for both waves of the FMHS. Additionally, the relationship between age and PSA level was assessed for each wave (solid and dotted lines on Figure 1). Measurements were consistent across age for both waves of the FMHS (Figure 1). The data and lines are nearly overlapping, indicating that there was no systematic change between the two measurements. This provided assurance that serum PSA levels for a given age were comparable for the two FMHS measurements.

COMMENT

In this study, we describe the distributions of changes in serum PSA levels in two populations of African-American and Caucasian men. African-American and Caucasian men in these cohorts had similar baseline serum PSA levels. However, the rates at which PSA levels changed differed substantially in these two populations. The annual percent change in PSA level in African-American men was approximately twice as high as it was in Caucasian men, regardless of baseline age.

Several studies have observed higher serum PSA levels in African-American men diagnosed with cancer⁷, however few studies have assessed longitudinal changes in serum PSA levels

in African-American men. McGreevy, et al., observed that the association between age and increasing PSA level differs for African-Americans and Caucasians in a group of men participating in a prostate cancer screening program, with more rapid changes observed in African-American men compared to Caucasian men⁹. Our data are consistent with these results, and suggest that African-American men have a much more rapid annual increase in PSA level compared to Caucasian men.

Loeb, et al.⁸ observed that men with PSA velocity of 0.4 ng/mL per year were significantly more likely to have adverse pathological features at radical prostatectomy, including positive surgical margins, seminal vesicle invasion, Gleason score 7 or greater, and higher tumor volume. In comparing the PSA levels from 1996 to 2000, a significantly greater proportion of African-American men in our cohort met this definition of PSA velocity of 0.4 ng/mL per year (8.7%) compared to their Caucasian counterparts (2.4%) ($P<0.001$). However, as also seen by McGreevy, et al.⁹, the estimated probabilities of converting to PSA greater than 4.0 ng/mL in our cohort were similar in both populations (4.9% in African-American men and 6.1% in Caucasian men; $P=0.61$). If the 0.4 ng/mL per year cut-point is used, more African-American men will be screened. If the 4.0 ng/mL cut-point is used, more Caucasian men will be screened. These findings underscore the clinical significance of these racial differences observed in PSA concentrations over time.

Racial disparities have been observed in prostate cancer incidence, stage, and mortality¹ and race has been shown to be an independent predictor of biochemical recurrence after radical prostatectomy¹⁸. It has also been suggested that diagnosing men earlier may mitigate differences in the stage of prostate cancer at diagnosis^{18,19}. With similar baseline PSA levels for African-Americans and Caucasians, it is possible that the higher rate of increase in PSA level over time for African-American men could be used to trigger a biopsy before an absolute PSA level cut-point is reached. As the baseline levels are low, after 4 years of follow-up, we would not expect to see differences in the number of men who exceed a cut-point of 4.0 ng/mL with the rates of change observed in these cohorts. Therefore, using the rate of change in PSA for screening in African-American men could potentially help to alleviate the racial disparities in prostate cancer diagnosis and mortality that currently exist.

To assess whether unknown measurement changes could account for the greater increases observed in the FMHS cohort compared to the OCS cohort, PSA measurements for each wave of the FMHS were assessed for their relationship with age and minimal differences were observed. For example, the average measurement for a 50-year-old at baseline was similar to the average measurement for a 50-year-old at follow-up. Similarly, there were minimal differences in the relationship of serum PSA level with age across the nine biennial rounds of the OCS study (data not shown). Additionally, the coefficient of variation was consistent during the OCS timeframe and we have observed comparability among the assays, at the lower levels of PSA seen in these cohorts. Therefore, it seems unlikely that the greater change over time observed in the FMHS was due to assay or measurement effects.

It is possible that the observed differences in the rate of change in serum PSA levels over time could be due to underlying biologic differences in prostate volumes between African-American and Caucasian men. We have previously seen a modest correlation between change in volume and change in PSA level in the OCS study²⁰. Therefore, more rapid prostate growth among African-American men may lead to more rapid changes in serum PSA levels. However, we and others have seen no significant differences in prostate volumes between African-American and Caucasian men^{21,22}. Additionally, adjustment for prostate volume did not change our results.

Men in the FMHS had higher body mass index (BMI) levels at baseline than men in the OCS cohort²³ and men with higher BMI levels have been observed to have lower serum PSA levels and lower rates of increase in PSA levels over time, possibly due to hemodilution²⁴. Because of this, we would have expected to see lower rates of PSA increase in African-American men compared to Caucasian men, but we saw the reverse. Additionally, adjustment for BMI did not change our study results.

Although some studies have questioned the utility of PSA velocity²⁵, others have found that PSA velocity may increase specificity in prostate cancer detection and identify those with worse outcomes^{5,26,27}. Since PSA velocity in men with cancer has been observed to be greater than in men without cancer^{5,8,28}, higher rates of change in PSA levels could be observed in African-American men if there are more undiagnosed cancers present. Both cohorts underwent thorough screening for prostate cancer, and all results in both cohorts were censored at the time of incident prostate cancer, medical (5-alpha reductase inhibitors) or surgical prostate treatments; therefore, a difference due to study design (where fewer cancers were detected in the FMHS population) should be minimal as both studies followed a similar protocol. In this study, we examined the natural history of annual changes in serum PSA levels by race; therefore PSA measurements prior to prostate treatment or diagnosis of prostate cancer were included and could increase the variability of our measurements. This is an appropriate approach, as one cannot determine *a priori* who will require treatment or be diagnosed with prostate cancer in the future.

There are several potential limitations that should be kept in mind. First, the intervals between examinations were two years for the OCS study and four years for the FMHS study. Thus, the data from these examinations may not provide accurate data for annual changes, which are often observed in clinical practice. There are only two time-points available from the FMHS, which leads to increased variability; however, results were similar when using empirical estimates of changes over time (data not shown). As the variability also decreases with increasing measurement interval, the estimate from this study most likely are a minimum estimate for changes one year apart. Additionally, we also observed that the median annualized percent change based on two points measured four years apart was similar to the median change estimated from 2-stage and longitudinal mixed models.

Finally, non-participation and drop-out during the course of the studies could introduce additional biases. An examination of the baseline characteristics and drop-out²⁹ from the OCS study indicated few differences. In the FMHS, there was greater participation in the clinic phase among men who reported greater lower urinary tract symptoms³⁰; however, this difference in participation did not bias the estimated age-specific reference ranges for PSA concentrations. Systematic differences, such as socioeconomic status and comorbidities, in the two populations may influence outcomes. In addition to these potential limitations, caution should be utilized when generalizing these findings to other races and ethnicity.

CONCLUSION

In conclusion, these population-based data describe the distribution of longitudinal changes in serum PSA levels in African-American and Caucasian men. These data suggest that African-American men have significantly more rapid rates of change in PSA levels over time. In light of the controversy surrounding PSA screening today, further work is needed to determine if PSA velocity as defined by percent change per year, could lead to earlier prostate cancer detection among African-American men. If the difference in rate of changes between African-American and Caucasian men is an early indicator of future prostate cancer

diagnosis, earlier detection in African-American men could help to diminish racial disparities in prostate cancer diagnosis and mortality.

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REFERENCES

1. Jemal A, Siegel R, Xu J, Ward E. Cancer Statistics, 2010. *Ca: a Cancer Journal for Clinicians*. 2010; 60:277–300.
2. Platz EA, Rimm EB, Willett WC, Kantoff PW, Giovannucci E. Racial variation in prostate cancer incidence and in hormonal system markers among male health professionals. *Journal of the National Cancer Institute*. 2000; 92:2009–2017. [PubMed: 11121463]
3. Henderson RJ, Eastham JA, Daniel JC, Whatley T, Mata J, Venable D, Kattan MW, Sartor O. Prostate-Specific Antigen (PSA) and PSA Density: Racial Differences in Men Without Prostate Cancer. *Journal of the National Cancer Institute*. 1997; 89:134–138.
4. Moul JW, Connelly RR, Mooneyhan RM, Zhang WEI, Sesterhenn IA, Mostofi FK, McLeod DG. Racial Differences in Tumor Volume and Prostate Specific Antigen Among Radical Prostatectomy Patients. *The Journal of Urology*. 1999; 162:394–397.
5. D'Amico AV, Chen MH, Roehl KA, Catalona WJ. Preoperative PSA velocity and the risk of death from prostate cancer after radical prostatectomy. *N Engl J Med*. 2004; 351:125–135. [PubMed: 15247353]
6. Berger AP, Deibl M, Steiner H, Bektic J, Pelzer A, Spranger R, Klocker H, Bartsch G, Horninger W. Longitudinal PSA changes in men with and without prostate cancer: assessment of prostate cancer risk. *Prostate*. 2005; 64:240–245. [PubMed: 15712213]
7. Thompson IM, Ankerst DP, Chi C, Goodman PJ, Tangen CM, Lucia MS, Feng Z, Parnes HL, Coltman CA Jr. Assessing prostate cancer risk: results from the Prostate Cancer Prevention Trial. *J Natl Cancer Inst*. 2006; 98:529–534. [PubMed: 16622122]
8. Loeb S, Roehl KA, Nadler RB, Yu X, Catalona WJ. Prostate specific antigen velocity in men with total prostate specific antigen less than 4 ng/ml. *J Urol*. 2007; 178:2348–2352. discussion 2352-3.
9. McGreevy K, Rodgers K, Lipsitz S, Bissada N, Hoel D. Impact of race and baseline PSA on longitudinal PSA. *Int J Cancer*. 2006; 118:1773–1776. [PubMed: 16231314]
10. Carter HB, Pearson JD, Waclawiw Z, Metter EJ, Chan DW, Guess HA, Walsh PC. Prostate-specific antigen variability in men without prostate cancer: effect of sampling interval on prostate-specific antigen velocity. *Urology*. 1995; 45:591–596. [PubMed: 7536366]
11. Chute CG, Panser LA, Girman CJ, Oesterling JE, Guess HA, Jacobsen SJ, Lieber MM. The prevalence of prostatism: a population-based survey of urinary symptoms. *J.Urol*. 1993; 150:85–89. [PubMed: 7685427]
12. Wei JT, Schottenfeld D, Cooper K, Taylor JM, Faerber GJ, Velarde MA, Bree R, Montie JE, Cooney KA. The natural history of lower urinary tract symptoms in black American men: relationships with aging, prostate size, flow rate and bothersomeness. *Journal of Urology*. 2001; 165:1521–1525.
13. Jacobsen SJ, Jacobson DJ, McGree ME, St Sauver JL, Klee GG, Girman CJ, Lieber MM. Sixteen-year longitudinal changes in serum prostate-specific antigen levels. The Olmsted County Study.
14. Laird NM, Ware JH. Random-effects models for longitudinal data. *Biometrics*. 1982; 38:963–974. [PubMed: 7168798]

15. Feldman HA. Families of lines: random effects in linear regression analysis. *J Appl Physiol.* 1988; 64:1721–1732. [PubMed: 3379003]
16. Oesterling JE, Jacobsen SJ, Chute CG, Guess HA, Girman CJ, Panser LA, Lieber MM. Serum prostate-specific antigen in a community-based population of healthy men. Establishment of age-specific reference ranges. *JAMA.* 1993; 270:860–864. [see comment].
17. Cooney KA, Strawderman MS, Wojno KJ, Doerr KM, Taylor A, Alcser KH, Heeringa SG, Taylor JM, Wei JT, Montie JE, et al. Age-specific distribution of serum prostate-specific antigen in a community-based study of African-American men. [Review] [20 refs]. *Urology.* 2001; 57:91–96. [PubMed: 11164150]
18. Parker PM, Rice KR, Sterbis JR, Chen Y, Cullen J, McLeod DG, Brassell SA. Prostate cancer in men less than the age of 50: a comparison of race and outcomes. *Urology.* 78:110–115. [PubMed: 21397300]
19. Resnick MJ, Canter DJ, Guzzo TJ, Brucker BM, Bergey M, Sonnad SS, Wein AJ, Malkowicz SB. Does race affect postoperative outcomes in patients with low-risk prostate cancer who undergo radical prostatectomy? *Urology.* 2009; 73:620–623. [PubMed: 19100607]
20. St Sauver JL, Jacobson DJ, Girman CJ, Lieber MM, McGree ME, Jacobsen SJ. Tracking of longitudinal changes in measures of benign prostatic hyperplasia in a population based cohort. *J.Urol.* 2006; 175:1018–1022. [PubMed: 16469608]
21. Sarma AV, Burke JP, Jacobson DJ, McGree ME, Sauver JST, Girman CJ, Lieber MM, Herman W, Macoska J, Montie JE, et al. Associations between diabetes and clinical markers of benign prostatic hyperplasia among community-dwelling black and white men. *Diabetes Care.* 2008; 31:476–482.
22. Mavropoulos JC, Partin AW, Amling CL, Terris MK, Kane CJ, Aronson WJ, Presti JC Jr, Mangold LA, Freedland SJ. Do racial differences in prostate size explain higher serum prostate-specific antigen concentrations among black men? *Urology.* 2007; 69:1138–1142. [PubMed: 17572202]
23. St Sauver JL, Sarma AV, Hollingsworth JM, Jacobson DJ, McGree ME, Dunn RL, Lieber MM, Jacobsen SJ. Associations Between Modest Weight Changes and Onset and Progression of Lower Urinary Tract Symptoms in Two Population-based Cohorts. *Urology.*
24. Wallner LP, Morgenstern H, McGree ME, Jacobson DJ, St Sauver JL, Jacobsen SJ, Sarma AV. The effects of body mass index on changes in prostate-specific antigen levels and prostate volume over 15 years of follow-up: implications for prostate cancer detection. *Cancer Epidemiol Biomarkers Prev.* 20:501–508. [PubMed: 21242331]
25. Vickers AJ, Till C, Tangen CM, Lilja H, Thompson IM. An empirical evaluation of guidelines on prostate-specific antigen velocity in prostate cancer detection. *Journal of the National Cancer Institute.* 2011; 103:462–469. [PubMed: 21350221]
26. Loeb S. Prostate cancer: Is PSA velocity useful? *Nature Reviews Urology.* 2009; 6:305–306.
27. Perrin P. PSA velocity and prostate cancer detection: the absence of evidence is not the evidence of absence. *Eur Urol.* 2006; 49:418–419. [PubMed: 16459016]
28. Carter HB, Pearson JD, Metter EJ, Brant LJ, Chan DW, Andres R, Fozard JL, Walsh PC. Longitudinal evaluation of prostate-specific antigen levels in men with and without prostate disease. *JAMA.* 1992; 267:2215–2220. [PubMed: 1372942]
29. Gades NM, Jacobson DJ, McGree ME, Lieber MM, Roberts RO, Girman CJ, Jacobsen SJ. Dropout in a longitudinal, cohort study of urologic disease in community men. *BMC.Med Res Methodol.* 2006; 6:58. [PubMed: 17169156]
30. Heeringa SG, Alcser KH, Doerr K, Strawderman M, Cooney K, Medbery B, Schottenfeld D. Potential selection bias in a community-based study of PSA levels in African-American men. *J Clin Epidemiol.* 2001; 54:142–148. [PubMed: 11166529]

Figure 1. Natural Log Transformed PSA Levels by Age at the Time of the Measurement (Flint Men's Health Study-Wave 1 And Wave 2). Lines Represent Modeled Smoothed Function of Natural Log Transformed PSA Level by Age for Each Wave.

Table 1

Baseline Distribution of Serum PSA Levels According to Age and Race. The Olmsted County Study of Urinary Symptoms and Health Status among Men & The Flint Men's Health Study.

Baseline age (years)	Caucasian Men			African-American Men		
	N	Median (25 th , 75 th percentile)	95 th percentile	N	Median (25 th , 75 th percentile)	95 th percentile
Overall	616	0.9 (0.6, 1.6)	4.1	150	0.9 (0.5, 1.5)	3.8
40–49	267	0.7 (0.5, 1.0)	1.8	49	0.8 (0.5, 1.3)	2.4
50–59	159	0.9 (0.6, 1.4)	2.9	47	0.8 (0.5, 1.3)	3.3
60–69	109	1.4 (0.8, 2.7)	4.6	37	1.1 (0.5, 1.8)	6.1
70+	81	2.1 (1.1, 3.3)	7.1	17	1.4 (1.0, 2.1)	5.6
						P value
						0.48
						0.43
						0.22
						0.19
						0.10

Distribution of Annualized Percent Change* in Serum PSA Level According to Age and Race. The Olmsted County of Urinary Symptoms and Health Status among Men & The Flint Men’s Health Study.

Table 2

Baseline age (years)	Caucasian Men			African-American Men		
	N	Mean	Standard Deviation	N	Mean	Standard Deviation
Overall	616	3.5	2.3	150	7.3	2.8
40–49	267	2.8	2.3	49	4.3	1.4
50–59	159	3.8	2.2	47	8.5	1.4
60–69	109	4.0	2.2	37	10.0	1.9
70+	81	4.6	1.7	17	6.7	1.8

* Annualized percent changes estimated from linear mixed-effects regression models.