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The Effect of Demographic and Clinical Factors on the Relationship Between BMI and PSA Levels

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Abstract

Introduction—Studies have reported lower prostate specific antigen (PSA) levels in men with a higher body mass index (BMI). Additional factors such as diabetes mellitus, benign prostatic hyperplasia (BPH) and certain medications may also affect PSA levels and confound the PSA-BMI association. In this study we evaluated the potential confounding effect of these factors on the obesity-PSA relationship and evaluated the association between these factors and PSA level.

Methods—The study cohort consisted of 770 population-based controls without a history of prostate cancer (PCa) who participated in a prior PCa study. Demographic, anthropometric and medical history data were obtained, and PSA level was determined from blood drawn at the time of interview. Linear regression was performed to evaluate the PSA-BMI relationship, adjusting for potential confounders. Finally, a forward stepwise algorithm was used to determine which factors were independently associated with PSA values.

Results—With increasing BMI (<25, 25–29, ≥30), the geometric mean PSA level declined (1.18, 1.13, and 0.94, respectively); obese men had a 17% (95% CI 0.70–0.99) lower age-adjusted PSA level compared to normal weight men. However, this relationship was non-significant (p=0.17) in the multivariate model. Independent predictors of PSA level included age (β=1.03, 95%CI 1.02–1.04), history of BPH (β=1.48, 95%CI 1.27–1.72), current statin (β=0.85, 95%CI 0.74–0.98) and NSAID use (β=0.84, 95%CI 0.72–0.98).

Conclusion—The relationship between obesity and PSA is confounded by a number of factors, which likely explain the observed inverse association previously reported. These results should help in interpreting PSA values in men screened for PCa.

Introduction

Prostate specific antigen (PSA) testing is routinely used along with digital rectal examination as a screening tool for prostate cancer (PCa). Threshold levels of PSA (e.g., >4.0 ng/mL), with or without consideration of age-specific effects,[1] are commonly used as an indication for prostate needle biopsy. Recently, research has shown that obesity is correlated with lower PSA levels,[2–10] with some investigators suggesting the use of different PSA thresholds based on body mass index (BMI).[4, 5, 9, 10]

In addition to age and obesity, a number of other factors may affect PSA values. These include diagnoses such as diabetes mellitus[11–13] and benign prostatic hyperplasia (BPH)[14],

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medication use (statins,[15–18] aspirin and other non-steroidal anti-inflammatory drugs (NSAIDs),[18–21] and thiazides[18]), race[22] and lifestyle factors such as low energy intake and use of high-dose calcium supplements.[23] A number of these factors often co-exist with obesity. However, most analyses have evaluated only the effect of an individual factor on PSA or with a limited number of other factors considered. Thus, the relative contribution of each of these factors, and whether they confound the observed PSA-obesity association, has not been fully explored. Using a population-based cohort of men without a history of PCa who provided detailed medical history data and blood samples, we investigated (1) whether the relationship between obesity and PSA is confounded by other factors; and (2) what factors are independently associated with PSA level.

Methods

Study participants

The study population consists of men without a self-reported history of PCa who participated in a population-based case-control study of PCa risk factors. Details of the study and data collection have been previously described.[15] The controls were male residents of King County, Washington identified using random digit telephone dialing and were recruited between 2002 – 2005. Complete household census information was obtained for 81% of the 24,106 residential telephone numbers contacted. Of eligible control men who were identified, 63% (n = 942) completed the study interview. Of these, 787 also provided a blood sample that was available for determination of PSA level.

Data Collection

Subjects completed in-person interviews conducted by trained interviewers. Information regarding demographic, lifestyle factors and medical history was collected. Diabetes mellitus and BPH diagnoses were self-reported as were height (maximum adult) and weight (one year prior to reference date) used for the BMI calculation. Men were asked about lifetime use of specific classes of medications, including statins, NSAIDs and aspirin before the reference date (a randomly assigned date that corresponded to the distribution of diagnosis dates of the PCa cases in the initial study). Subjects were asked “which of these medications did you take at least once a week for three months or longer” along with dates of starting and stopping the medication for each episode of use. Men were also asked about use of several other medications, including thiazides (ever/never). PSA level (in ng/mL) was determined from stored plasma using the Abbott Laboratories IMx Total PSA microparticle enzyme immunoassay.

Statistical Analysis

BMI was categorized as normal weight (<25 kg/m^2), overweight (25–29) and obese (≥30). Men taking finasteride (n = 17) at reference date were excluded. The distributions of demographic and clinical factors by BMI were compared with Chi-squared tests. Current medication use was defined by use at reference date. We examined aspirin and other NSAIDs separately and combined. Since PSA values were non-normally distributed, the PSA data were log-transformed. The geometric mean PSA was determined for men in each category of demographic and clinical factors analyzed. The ratio of the geometric means (RGM) was determined with linear regression. All geometric output was exponentiated back for reporting.

Analysis 1—To determine if the obesity-PSA relationship is confounded by other factors, a base model including only age and BMI was constructed. We then evaluated each of the variables available that has been suggested to affect PSA levels to determine which should be included in the final model as confounders. These variables (family history of PCa, race,

diabetes mellitus, BPH, and medication use (statin, aspirin and other NSAIDs (both considered separately and together), and thiazides)) were added one at a time to the base model, and a variable was considered to be a confounder if it changed the risk estimate for BMI by ≥ 5%. The variable with the strongest effect was then added to the base model and the other variables from the first round that were confounders were successively added to this new base model. This was repeated until no further variables changed the risk estimate for BMI by ≥ 5%. An additional model was constructed where all potential variables *a priori* thought to affect the PSA-obesity association were included in the model. Finally, as obesity may lead to BPH and subsequently higher PSA levels, we performed additional analyses with (1) BPH excluded from the model and (2) in men without BPH.

Analysis 2—To determine if variables were independently associated with PSA value, a forward stepwise algorithm was performed. The age-adjusted model served as the base model, and the same variables as above were separately added. Each incremental model was then compared to the base model with the likelihood ratio test, and significant variables were those with a p-value ≤ 0.05. The variable with the strongest effect was then added to the base model and the other significant variables from the first round were successively added to this new base model. This was repeated until no further variables significantly improved the model. Potential interaction between the variables in the final model was evaluated with the likelihood ratio test. All statistical analyses were conducted using Stata software, Version 10 (Stata, Inc., College Station, TX).

Results

A total of 770 men with PSA data were available for the analysis. In Table 1, the geometric mean PSA levels are shown by different characteristics along with the corresponding age-adjusted RGMs. As expected, increasing age was associated with an increase in geometric mean PSA. A family history of PCa (RGM= 1.27, 95% CI 1.04 – 1.54) and a history of BPH (RGM= 1.45, 95% CI 1.25 – 1.70) also were associated with an increase in the age-adjusted geometric mean PSA level. Current use of aspirin alone (RGM 0.88, 95% CI 0.77 – 1.00) and use of aspirin combined with other NSAIDs (RGM 0.84, 95% CI 0.73 – 0.95) were associated with lower geometric mean PSA levels in age-adjusted models. Non-significant decreases in PSA were observed for men with a history of diabetes and those who used non-aspirin NSAIDs alone or thiazides.

In Table 2, the distributions of demographic and medical history factors by BMI category are shown. Diabetes mellitus and current statin use were both more common in overweight and obese men relative to those with a BMI of <25. African-American men had higher BMIs compared to Caucasian men. Ever use of a thiazide and current non-aspirin NSAID use were more common in men with higher BMIs, but these differences were not statistically significant (p-values > 0.05). The prevalence of current statin use and aspirin use varied by age. Statin use rose in each age group from < 10% for those aged 40–49 years, to 35% for those aged 70–74 years. Aspirin use also rose from 15% in the youngest age group to greater than 60% in those over 65 years of age or older. Current usage of non-aspirin NSAIDs did not vary substantially by age.

Table 3 shows the unadjusted, age-adjusted and multivariate adjusted results for the association between BMI and PSA levels. In the age-adjusted model, obese men (BMI ≥ 30) had a 17% reduction in mean PSA compared to normal weight men (95% CI 0.70 – 0.99, p-trend= 0.04). In building the multivariate model, BPH had the strongest effect on the relationship between BMI and PSA. Statin use had the next largest effect on the BMI-PSA relationship, followed by diabetes mellitus and any NSAIDs use (aspirin or other NSAIDs). After adjustment for these confounding factors the relationship between BMI and PSA level

was no longer significant (p = 0.17). Race, family history of PCa and thiazide use did not significantly change the estimate for BMI and were not included in this model. In the *a priori* model, where all variables were included, the relationship between BMI and PSA was also non-significant (p = 0.16). Finally, exclusion of BPH from the model and limiting the analysis to those men without BPH did not alter the results (data not shown).

The variables that were independently associated with geometric mean PSA level were age, BPH, statin use and any NSAIDs (aspirin or other NSAIDs) use. A multivariate model was created using these variables. A history of BPH was associated with a 48% increase in the geometric mean PSA (95% CI 1.27 – 1.72). The use of statins (RGM 0.85, 95% CI 0.74 – 0.98) or any NSAIDs (RGM 0.84, 95% CI 0.72 – 0.98) were both associated with an approximately 15% decrease in PSA. There was only a weak correlation between NSAID use and statin use (r^2=0.34). There was no evidence for interaction between any of the variables in the final model (all likelihood ratio p-values > 0.05). None of the other variables, including BMI, were associated independently with PSA levels.

Discussion

In this population-based cohort of men without a history of PCa, we evaluated demographic and medical history factors for their potential correlation with plasma PSA levels. Similar to prior reports, we found an inverse relationship between BMI and PSA whereby obesity is correlated with lower PSA values. This association, however, was no longer significant when analyses were adjusted for confounding factors (age, current statin use, current aspirin or other NSAID use, diabetes mellitus and BPH). In addition, we identified several factors other than BMI that were independently associated with PSA levels.

A relationship between obesity and lower PSA levels has been found in a number of reports,[2–10] but it is not a consistent finding across all studies.[12, 24–26] One of the prevailing theories to explain this BMI-PSA relationship is that hemodilution from greater total plasma volume in obese men results in lower PSA levels.[2, 3, 5] Based on this notion, several investigators have recently proposed that BMI-adjusted PSA levels be used for PCa screening.[4, 5, 9, 10] Although we observed a 17% lower geometric mean PSA in obese men relative to normal weight men when adjusting only for age (95% CI 0.70 – 0.99), this association was not significant (p = 0.17) after adjustment for the confounding effects of BPH, diabetes mellitus, and current statin and NSAID/aspirin use.

After finding that the obesity-PSA association was confounded by other factors, we evaluated other variables for an independent association with PSA levels. Four factors were significantly associated with PSA level: age, history of BPH, current statin use, and current use of any any NSAIDs (aspirin or other NSAIDs). Both age and a history of BPH were positively associated with PSA levels, which is consistent with earlier reports.[1, 14] The association between use of statins with PSA levels has been previously investigated, as these medications have also been suggested to reduce the risk of PCa.[17, 27] In a longitudinal study of men from a Veterans Affairs Medical Center, use of a statin for up to one year was associated with a 4.1% decline in PSA.[28] In our study, current statin use was associated with a 16% lower geometric mean PSA, and statin use was more commonly reported by overweight and obese men (27%) compared to normal weight men (19%, p = 0.04). The mechanism by which statin use lowers PSA is unknown. Statins are involved in cholesterol metabolism and there is evidence that levels of cholesterol in prostatic tissue may be related to malignant cell proliferation and metabolism.[29] Statins have also been shown to promote apoptosis and inhibit growth of PCa cells.[30] Finally, it has recently been shown that non-cancerous prostate cell lines have reduced growth in the presence of statins[31], and statin use has been associated with smaller prostate size.[32]

Use of NSAIDs and aspirin has also been associated with lower PSA levels[18–20] and studied as a potential chemoprevention of PCa.[21, 33, 34] As with statins, the mechanism(s) through which NSAIDs may reduce PSA is unknown, but includes anti-inflammation activity from COX inhibition,[35] reduced angiogenesis[36] and induction of apoptosis.[37] In our study, current use of aspirin and use of other NSAIDs were associated with lower geometric PSA levels in age-adjusted models, but not in multivariate models. However, when these medications were combined in the analysis, PSA levels were 15% lower for those currently taking any aspirin and/or other NSAID compared to non-users (95% CI 0.74 – 0.98).

One strength of this study was the ability to evaluate multiple factors that may be correlated with BMI and PSA levels. Many of the published studies that have evaluated the relationship between obesity and PSA adjusted results only for age and race,[5–7] or additionally included prostate size.[2, 10] However, analyses from the PLCO screening trial[3] and from the placebo arm of the PCPT trial[23] included additional factors. A history of BPH and a family history of PCa were included in the analysis from the PLCO study, although no estimates of the association between these factors and PSA values were provided.[3] In the PCPT cohort analysis by Kristal et al., smoking, physical activity and dietary intake were also considered in relation to PSA levels.[23] Another study that explored use of NSAIDs and the correlation with PSA levels adjusted for age, race, family history of PCa, BPH and diabetes mellitus, however this was in a cohort of men undergoing prostate needle biopsy.[19] Similar to our study, other PSA and obesity studies have used population-based samples, including a study by Baillargeon et al. that only adjusted for age and race,[6] and two from NHANES.[13, 20] The NHANES studies were focused on the relationships between diabetes mellitus[13] and statin use[20] with PSA and did not include the same variables considered in our analyses.

There are some limitations to our study that should be considered when interpreting results. We relied on self-reported medical history and medication use collected as part of an in-person interview. In a separate analysis of a subset of this study population that was designed to validate use of statin medications, there was 87% agreement between self-reported use and computerized pharmacy records.[15] Given that aspirin and other NSAIDs are primarily over-the-counter, self-reports may provide more complete exposure data than pharmacy records. We also used self-reported data on a history of BPH, however the prevalence of BPH from our study population (age < 50: prevalence of BPH 7%; 50–59: 13%, 60–69: 27%; ≥70: 39%) is consistent with other epidemiologic studies.[38–40] We could not distinguish Type I from Type II diabetes mellitus and this may have impacted our evaluation of the effect of diabetes on PSA levels. However, early onset Type I is rare, and only two men reported being diagnosed with diabetes before age 18 and exclusion of these men did not change the results. Only a single PSA measurement was obtained, which may not be as reliable as multiple PSA measures. We also used self-reported anthropometric data, which are less reliable that measured ones, although studies have found that self-reported anthropometric data are reliable in epidemiologic studies of biomarkers.[41] Finally, as our data are cross-sectional, we cannot show causality but rather only demonstrate observed associations between the PSA value and the other variables at a given point in time.

In conclusion, this analysis of data from a population-based cohort of men without a diagnosis of PCa found that several factors confound the previously reported BMI-PSA association. Once these factors were accounted for in the analysis, there was no significant relationship between obesity and PSA level. In addition, we identified several factors that were independently associated with PSA level. Our research along with that from other groups supports the need for considering multiple factors when interpreting PSA values used to guide decisions about the need for prostate biopsy.

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References

1. Oesterling JE, Jacobsen SJ, Chute CG, et al. Serum prostate-specific antigen in a community-based population of healthy men. Establishment of age-specific reference ranges. Jama. Aug 18; 1993 270(7):860–864. [PubMed: 7688054]
2. Banez LL, Hamilton RJ, Partin AW, et al. Obesity-related plasma hemodilution and PSA concentration among men with prostate cancer. Jama. Nov 21; 2007 298(19):2275–2280. [PubMed: 18029831]
3. Grubb RL 3rd, Black A, Izmirlian G, et al. Serum prostate-specific antigen hemodilution among obese men undergoing screening in the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial. Cancer Epidemiol Biomarkers Prev. Mar; 2009 18(3):748–751. [PubMed: 19258472]
4. Price MM, Hamilton RJ, Robertson CN, Butts MC, Freedland SJ. Body mass index, prostate-specific antigen, and digital rectal examination findings among participants in a prostate cancer screening clinic. Urology. May; 2008 71(5):787–791. [PubMed: 18267334]
5. Rundle A, Neugut AI. Obesity and screening PSA levels among men undergoing an annual physical exam. Prostate. Mar 1; 2008 68(4):373–380. [PubMed: 18189231]
6. Baillargeon J, Pollock BH, Kristal AR, et al. The association of body mass index and prostate-specific antigen in a population-based study. Cancer. Mar 1; 2005 103(5):1092–1095. [PubMed: 15668913]
7. Werny DM, Thompson T, Saraiya M, et al. Obesity is negatively associated with prostate-specific antigen in U.S. men, 2001–2004. Cancer Epidemiol Biomarkers Prev. Jan; 2007 16(1):70–76. [PubMed: 17179487]
8. Culp S, Porter M. The effect of obesity and lower serum prostate-specific antigen levels on prostate-cancer screening results in American men. BJU Int. Nov; 2009 104(10):1457–1461. [PubMed: 19522868]
9. Hekal IA, Ibrahiem EI. Obesity-PSA relationship: a new formula. Prostate Cancer Prostatic Dis. Dec 22.2009
10. Loeb S, Carter HB, Schaeffer EM, Ferrucci L, Kettermann A, Metter EJ. Should prostate specific antigen be adjusted for body mass index? Data from the Baltimore Longitudinal Study of Aging. J Urol. Dec; 2009 182(6):2646–2651. [PubMed: 19836806]
11. Fukui M, Tanaka M, Kadono M, et al. Serum prostate-specific antigen levels in men with type 2 diabetes. Diabetes Care. May; 2008 31(5):930–931. [PubMed: 18276768]
12. Muller H, Raum E, Rothenbacher D, Stegmaier C, Brenner H. Association of diabetes and body mass index with levels of prostate-specific antigen: implications for correction of prostate-specific antigen cutoff values? Cancer Epidemiol Biomarkers Prev. May; 2009 18(5):1350–1356. [PubMed: 19383895]
13. Werny DM, Saraiya M, Gregg EW. Prostate-specific antigen values in diabetic and nondiabetic US men, 2001–2002. Am J Epidemiol. Nov 15; 2006 164(10):978–983. [PubMed: 17023544]
14. Carter HB, Pearson JD, Metter EJ, et al. Longitudinal evaluation of prostate-specific antigen levels in men with and without prostate disease. Jama. Apr 22–29; 1992 267(16):2215–2220. [PubMed: 1372942]
15. Agalliu I, Salinas CA, Hansten PD, Ostrander EA, Stanford JL. Statin use and risk of prostate cancer: results from a population-based epidemiologic study. Am J Epidemiol. Aug 1; 2008 168(3):250–260. [PubMed: 18556686]
16. Cyrus-David MS, Weinberg A, Thompson T, Kadmon D. The effect of statins on serum prostate specific antigen levels in a cohort of airline pilots: a preliminary report. J Urol. Jun; 2005 173(6): 1923–1925. [PubMed: 15879782]

17. Platz EA, Leitzmann MF, Visvanathan K, et al. Statin drugs and risk of advanced prostate cancer. J Natl Cancer Inst. Dec 20; 2006 98(24):1819–1825. [PubMed: 17179483]

18. Chang SL, Harshman LC, Presti JC Jr. Impact of common medications on serum total prostate-specific antigen levels: analysis of the National Health and Nutrition Examination Survey. J Clin Oncol. Sep 1; 2010 28(25):3951–3957. [PubMed: 20679596]

19. Fowke JH, Motley SS, Smith JA Jr, et al. Association of nonsteroidal anti-inflammatory drugs, prostate specific antigen and prostate volume. J Urol. May; 2009 181(5):2064–2070. [PubMed: 19286210]

20. Singer EA, Palapattu GS, van Wijngaarden E. Prostate-specific antigen levels in relation to consumption of nonsteroidal anti-inflammatory drugs and acetaminophen: results from the 2001–2002 National Health and Nutrition Examination Survey. Cancer. Oct 15; 2008 113(8):2053–2057. [PubMed: 18780337]

21. Platz EA, Rohrmann S, Pearson JD, et al. Nonsteroidal anti-inflammatory drugs and risk of prostate cancer in the Baltimore Longitudinal Study of Aging. Cancer Epidemiol Biomarkers Prev. Feb; 2005 14(2):390–396. [PubMed: 15734963]

22. Morgan TO, Jacobsen SJ, McCarthy WF, Jacobson DJ, McLeod DG, Moul JW. Age-specific reference ranges for prostate-specific antigen in black men. N Engl J Med. Aug 1; 1996 335(5): 304–310. [PubMed: 8663870]

23. Kristal AR, Chi C, Tangen CM, Goodman PJ, Etzioni R, Thompson IM. Associations of demographic and lifestyle characteristics with prostate-specific antigen (PSA) concentration and rate of PSA increase. Cancer. Jan 15; 2006 106(2):320–328. [PubMed: 16342294]

24. Hutterer G, Perrotte P, Gallina A, et al. Body mass index does not predict prostate-specific antigen or percent free prostate-specific antigen in men undergoing prostate cancer screening. Eur J Cancer. May; 2007 43(7):1180–1187. [PubMed: 17292604]

25. Ku JH, Kim ME, Lee NK, Park YH, Ahn JO. Influence of age, anthropometry, and hepatic and renal function on serum prostate-specific antigen levels in healthy middle-age men. Urology. Jan; 2003 61(1):132–136. [PubMed: 12559283]

26. Capitanio U, Perrotte P, Hutterer GC, et al. Effect of body mass index on prostate-specific antigen and percentage free prostate-specific antigen: results from a prostate cancer screening cohort of 1490 men. Int J Urol. Jan; 2009 16(1):91–95. [PubMed: 19054167]

27. Jacobs EJ, Rodriguez C, Bain EB, Wang Y, Thun MJ, Calle EE. Cholesterol-lowering drugs and advanced prostate cancer incidence in a large U.S. cohort. Cancer Epidemiol Biomarkers Prev. Nov; 2007 16(11):2213–2217. [PubMed: 17971518]

28. Hamilton RJ, Goldberg KC, Platz EA, Freedland SJ. The influence of statin medications on prostate-specific antigen levels. J Natl Cancer Inst. Nov 5; 2008 100(21):1511–1518. [PubMed: 18957682]

29. Solomon KR, Freeman MR. Do the cholesterol-lowering properties of statins affect cancer risk? Trends Endocrinol Metab. May-Jun;2008 19(4):113–121. [PubMed: 18356074]

30. Hoque A, Chen H, Xu XC. Statin induces apoptosis and cell growth arrest in prostate cancer cells. Cancer Epidemiol Biomarkers Prev. Jan; 2008 17(1):88–94. [PubMed: 18199714]

31. Murtola TJ, Pennanen P, Syvala H, Blauer M, Ylikomi T, Tammela TL. Effects of simvastatin, acetylsalicylic acid, and rosiglitazone on proliferation of normal and cancerous prostate epithelial cells at therapeutic concentrations. Prostate. Jun 15; 2009 69(9):1017–1023. [PubMed: 19301305]

32. Fowke JH, Motley SS, Barocas DA, et al. The associations between statin use and prostate cancer screening, prostate size, high-grade prostatic intraepithelial neoplasia (PIN), and prostate cancer. Cancer Causes Control. Dec 19.2010

33. Roberts RO, Jacobson DJ, Girman CJ, Rhodes T, Lieber MM, Jacobsen SJ. A population-based study of daily nonsteroidal anti-inflammatory drug use and prostate cancer. Mayo Clin Proc. Mar; 2002 77(3):219–225. [PubMed: 11888024]

34. Jacobs EJ, Rodriguez C, Mondul AM, et al. A large cohort study of aspirin and other nonsteroidal anti-inflammatory drugs and prostate cancer incidence. J Natl Cancer Inst. Jul 6; 2005 97(13):975–980. [PubMed: 15998950]

35. Stock D, Groome PA, Siemens DR. Inflammation and prostate cancer: a future target for prevention and therapy? Urol Clin North Am. Feb; 2008 35(1):117–130. vii. [PubMed: 18061030]

36. Wang W, Bergh A, Damber JE. Cyclooxygenase-2 expression correlates with local chronic inflammation and tumor neovascularization in human prostate cancer. Clin Cancer Res. May 1; 2005 11(9):3250–3256. [PubMed: 15867220]

37. Yoo J, Lee YJ. Aspirin enhances tumor necrosis factor-related apoptosis-inducing ligand-mediated apoptosis in hormone-refractory prostate cancer cells through survivin down-regulation. Mol Pharmacol. Dec; 2007 72(6):1586–1592. [PubMed: 17848598]

38. Chute CG, Panser LA, Girman CJ, et al. The prevalence of prostatism: a population-based survey of urinary symptoms. J Urol. Jul; 1993 150(1):85–89. [PubMed: 7685427]

39. Trueman P, Hood SC, Nayak US, Mrazek MF. Prevalence of lower urinary tract symptoms and self-reported diagnosed ‘benign prostatic hyperplasia’, and their effect on quality of life in a community-based survey of men in the UK. BJU Int. Mar; 1999 83(4):410–415. [PubMed: 10210562]

40. Norman RW, Nickel JC, Fish D, Pickett SN. ‘Prostate-related symptoms’ in Canadian men 50 years of age or older: prevalence and relationships among symptoms. Br J Urol. Nov; 1994 74(5): 542–550. [PubMed: 7530115]

41. McAdams MA, Van Dam RM, Hu FB. Comparison of self-reported and measured BMI as correlates of disease markers in US adults. Obesity (Silver Spring). Jan; 2007 15(1):188–196. [PubMed: 17228047]

Table 1

Geometric mean PSA and age-adjusted ratio of geometric mean (RGM) PSA in a population-based cohort of men from King County, WA

	N	Geometric Mean	RGM (95% CI)
Age			
40 – 49	75	0.68	1.00 (referent)
50 – 54	93	0.83	1.23 (0.94 – 1.61)
55 – 59	149	0.94	1.39 (1.08 – 1.78)
60 – 64	152	1.13	1.66 (1.30 – 2.13)
65 – 69	163	1.14	1.68 (1.32 – 2.14)
70 – 74	138	1.83	2.70 (2.10 – 3.46)
BMI category			
Normal (< 25)	219	1.18	1.00 (referent)
Overweight (25 – 29)	363	1.13	0.96 (0.83 – 1.11)
Obese (≥ 30)	188	0.94	0.83 (0.70 – 0.99)
Race			
Caucasian	704	1.10	1.00 (referent)
African-American	66	0.99	1.17 (0.93 – 1.49)
Family history of prostate cancer[+]			
No	679	1.06	1.00 (referent)
Yes	91	1.34	1.27 (1.04 – 1.54)
Diabetes mellitus			
No	693	1.10	1.00 (referent)
Yes	77	1.00	0.85 (0.69 – 1.05)
BPH [*]			
No	599	0.97	1.00 (referent)
Yes	171	1.63	1.45 (1.25 – 1.70)
Statin use (current)			
No	578	1.10	1.00 (referent)
Yes	192	1.06	0.83 (0.72 – 0.97)
Aspirin use (current)			
No	415	1.06	1.00 (referent)
Yes	355	1.13	0.88 (0.77 – 1.00)
other NSAID use (current)			
No	665	1.03	1.00 (referent)
Yes	105	0.96	0.85 (0.71 – 1.02)
Aspirin or other NSAID use (current)			
No	364	1.08	1.00 (referent)
Yes	406	1.10	0.84 (0.73 – 0.95)
Thiazide use			
No	704	1.10	1.00 (referent)
Yes	66	1.00	0.85 (0.68 – 1.06)

[+] First-degree relative with prostate cancer

[*] Self-reported history of a physician's diagnosis of benign prostatic hyperplasia

Table 2

Body mass index (BMI) stratified by selected demographic and medical history factors in a population-based cohort of men from King County, WA

Characteristic	BMI Category			p-value
	< 25	25 – 29.9	≥ 30	
	N (%)	N (%)	N (%)	
Age				
40 – 49	22 (10.0)	34 (9.4)	19 (10.1)	0.30
50 – 54	26 (11.9)	46 (12.7)	21 (11.1)	
55 – 59	43 (19.6)	65 (17.9)	41 (21.8)	
60 – 64	34 (15.5)	71 (19.6)	45 (25.0)	
65 – 69	47 (21.5)	78 (21.5)	38 (20.2)	
70 – 74	47 (21.5)	69 (19.0)	22 (11.7)	
Race				
Caucasian	203 (92.7)	338 (93.1)	163 (86.7)	0.03
African-American	16 (7.3)	25 (6.9)	25 (13.3)	
Family history of prostate cancer[+]				
No	192 (87.7)	314 (86.5)	173 (92.0)	0.16
Yes	27 (12.3)	49 (13.5)	15 (8.0)	
Diabetes mellitus				
No	209 (95.4)	333 (91.7)	151 (80.3)	< 0.001
Yes	10 (4.6)	30 (8.3)	37 (19.7)	
BPH[*]				
No	163 (74.4)	282 (77.7)	154 (81.9)	0.19
Yes	56 (25.6)	81 (22.3)	34 (18.1)	
Statin use (current)				
No	178 (81.3)	261 (71.9)	139 (73.9)	0.04
Yes	41 (18.7)	102 (28.1)	49 (26.1)	
Aspirin use (current)				
No	124 (56.6)	186 (51.2)	105 (55.9)	0.34
Yes	95 (43.4)	177 (48.8)	83 (44.2)	
Other NSAID use (current)				
No	197 (90.0)	314 (86.5)	154 (81.9)	0.06
Yes	22 (10.0)	49 (13.5)	34 (18.1)	
Aspirin or Other NSAID use (current)				
No	112 (51.1)	162 (44.6)	90 (47.9)	0.31
Yes	107 (48.9)	201 (55.4)	98 (52.1)	
Thiazide use				
No	208 (95.0)	329 (90.6)	167 (88.8)	0.07
Yes	11 (5.0)	34 (9.4)	21 (11.2)	

[+] First-degree relative diagnosed with prostate cancer

[*] Self-reported history of a physician's diagnosis of benign prostatic hyperplasia

Table 3

Linear regression models of geometric mean PSA by body mass index in a population-based cohort of men from King County, WA

	Body Mass Index			
	< 25	**25 – 29.9**	**≥ 30**	**p-trend**
		RGM (95% CI)	**RGM (95% CI)**	
Unadjusted	1.00 (referent)	0.95 (0.81 – 1.11)	0.79 (0.66 – 0.95)	0.01
Age-Adjusted	1.00 (referent)	0.96 (0.83 – 1.11)	0.83 (0.70 – 0.99)	0.04
Multivariate*	1.00 (referent)	1.00 (0.86 – 1.16)	0.88 (0.74 – 1.05)	0.17

*Adjusted for age, current statin use, current aspirin or other NSAID use, diabetes mellitus and benign prostatic hyperplasia.