Does a Delayed Cull Phenomenon Explain the Discrepancy in PSA Scores Among African American Men and European American Men?

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By
Megan Lutz

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Abstract:

As would be expected of a successful screening method, the initiation of the prostate-specific antigen (PSA) screening test effectively detected more cases of prostate cancer in the early 90s, and the incidence appeared to increase shortly after PSA test introduction. Since its introduction as a trusted prostate cancer (PCa) screening method in 1986, the incidence of PCa reportedly rose rather abruptly, peaked in 1992, and subsequently plateaued near its initial lower incidence; this pattern is known as the Cull Phenomenon. Because African Americans as a whole present with a higher incidence of prostate cancer and because they only represent a fraction of the screened prostate population compared to European Americans, we question whether or not the currently reported Cull Phenomenon expresses true African American incidence over time. These disparities have been attributed to genetics and factors associated with socioeconomic status, such as limited healthcare access, literacy, and dietary factors. We conducted this retrospective study because we hypothesized that a delayed Cull Phenomenon due to limited health care access for African American men is responsible for elevated PSA and prostate cancer incidence. Between the early and late nineties the incidence of cancer became more significantly greater than that of whites, suggesting a possible delayed Cull Phenomenon. But overall the actual African American incidence decreased from 60% to 49.6% over time, their severity, or grade, of cancer decreased from 7.18 to 6.66 over time, and the PSA of cancerous men also decreased from 21.91 to 12.94, all of which decreases indicate that African American men seem to be represented by the Cull Phenomenon currently reported. Further, we attribute these African American improvements to increased screening awareness within the Cleveland community.
Acknowledgments

Primarily, I would like to thank Jeannette Potts for what has been gained beyond our teamwork on this study. I value her specific and articulate and attention to life, what she has taught me, and the ways she has contributed to my outlook on life. In many ways, we are kindred spirits.

I also believe that Miami University’s Honors Program is a gift to the students offering a completely unique experience from the rest of the campus. When appreciated for what this program is, a student’s learning experience becomes a more self-empowering, self-seeking experience, and in life, this is what learning is all about. I thank the Honors Program for their financial assistance throughout the research and printing of my thesis and for their varieties of support expressed in the conglomeration of staff.

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Background:

To date, a preponderance of evidence indicates that the incidence (3, 18, 36) and grade, or severity, (24, 11) of prostate cancer (PCa) among African American men (AA) are greater than that of European Americans (EA). Further, these two discrepancies are directly supported by the disparity in the scores of the Prostate-Specific Antigen (PSA) exam, the screening test for prostate cancer. PSA levels of AA men are significantly higher than the rest of the population (9, 36, 11). This general racial discrepancy is also noticed in other forms of cancer, such as breast (16, 5) and cervical cancers (6), but is not observed in skin cancer (12). Numerous studies have been conducted throughout multiple forms of cancer and specifically within the factors associated with prostate cancer to support a racial disparity. However, our study is more unique in that it examines the factors surrounding PCa, how they vary by race, and how they change over time to conclude that in multiple ways, the racial differences are being improved simply by an increased access to healthcare, indicating that genetics may not be as responsible for these differences as purported. The results of our Cleveland study are also corroborated by another study which concluded that when given the same access to healthcare, this racial disparity disappears (2).

Genetic factors and/or socioeconomic related factors may be responsible for the disparity in prostate cancer incidence and grade and PSA. One genetic factor is increased serum testosterone levels in AA men (13). It is theorized that the conversion of testosterone to its active form, dihydrotestosterone, enables the progression of prostate disease. This is the mechanism by which many prostate quieting drugs work. Proscar and Finasteride are alpha 5 reductase inhibitors, which prevent this conversion and are
administered to prevent growth of the prostate in Benign Prostatic Hyperplasia (BPH) patients. Secondly, the presence of shorter CAG repeats in the androgen receptor of the African American genome (13, 25) have been investigated. CAG repeats may either work to enhance reception of testosterone or may facilitate progression independent of testosterone levels. Additional genetic avenues researched include increased intensity of the gene, EZH2’s, activity (33) and stronger linkage to the marker for Chromosome 1q, HPC11 (20).

In addition to genetic variables, much emphasis has been placed on varying factors associated with socioeconomic status and race (31) that potentially contribute to a difference in PSA scores. African Americans as a group consume more fatty foods high in cholesterol than the diet associated with European Americans, and diet may play a role in the increased PSA (1, 21, 31). Religion, marital status, occupational factors, tobacco consumption, and alcohol consumption also are embodied in the socioeconomic status (SES) hypothesis (31). The still present lower literacy among the AA community in comparison with other races may likely contribute to decreased health awareness (1, 17). Finally, it is possible that limited healthcare access has inhibited African American men from regularly monitoring PSA levels and detecting early cancer growth, thus enabling the undetected increase in PSA and onset of PCa (7).

Tarman et al examined socioeconomic status within the military by differentiating between officer and enlisted men as well as by race, specifically noting that within the military, access to healthcare is equal for race and rank. This study found that enlisted men, or men of a lower socioeconomic status, had greater prostate cancer progression, and that race was not predictive of cancer grade. However, it was found that
African American men more often had biochemical recurrence after radical prostatectomy. Although a greater percentage of AA men made up the enlisted population than the officer population, the conclusions of this study found that race, independent of SES and access, was predictive of recurrence. Tarman et al concluded that a racial difference supercedes any socioeconomic disparities with respect to prostate cancer.

An interesting aspect of health care and the African American community was re-addressed in a study by Powell et al (1996). The Tuskegee Syphilis Study from 1932 to 1972 denied 399 poor AA men medical care for their syphilis in Tuskegee, Alabama. Instead, the physicians chose to observe the progression of their diseased state in order to learn more about syphilis, even despite the introduction of penicillin after World War II. As a result, a tremendous rift of mistrust separates the AA and scientific community and has distanced the two communities for the past 30 years. Such hurt has evoked resistance not only to participation in scientific research, but also to health education (20). Thus, with respect to prostate cancer, this scarred community has possibly shied away from screening, biopsy, and treatment of the disease, which prevents the surge seen in the cull phenomenon of the Caucasian race.

The PSA Exam

Prostate Specific Antigen (PSA) is a serine protease released into the blood by both benign and malignant prostatic epithelium that can be quantified in serum samples via immunoassay. This quantification is known as the PSA exam. Elevated amounts of PSA released into the blood indicate abnormal functioning in the prostate; and at a PSA
of 4, the Cleveland Clinic advises prostate biopsies. Typically, doctors begin tabulating men’s PSA at the age of fifty and develop a baseline of PSA scores to establish personal norms. Depending on family history, PSA testing may begin at a younger age; and it has been suggested in multiple age-race related studies (9, 22, 35) that each race should begin testing at different ages. Primarily, since AA men seem to not only have higher PSA scores, but also seem to have PSA scores that increase at a more rapid rate, earlier testing may be beneficial to their early treatment (22).

Although it is currently the most widely accepted screening method since its initiation in 1986, the PSA exam is not the only tool for risk assessment. Because the sensitivity and specificity of this technique are frequently criticized, the Digital Rectal Exam is used in conjunction to enhance the positive prediction of prostate cancer by determining the potential presence of tumors typical of prostate cancer. Likewise, the results of our study indicate that other factors such as age, inflammation, and Prostatic Intraepithelial Neoplasia (PIN) enhance the predictability of prostate cancer, more so for AA men than EA men. Variables unexplored by our study, but substantially examined elsewhere are the EXH2 gene’s predictive abilities (33), PSA doubling time as a measure of disease progression (28), rate of change of PSA to observe disease progression before and after cancer diagnosis (7), and monitoring extracapsular extension to stratify clinical stage (23).

Further, an elevated PSA does not point exclusively towards prostate cancer, which is why a more definitive marker would be helpful. Elevated PSA indicates abnormal prostate functioning, which could include several abnormalities. The other major explanation for elevated PSA is Benign Prostatic Hyperplasia. While it has been a
problem that too many men have been biopsied to find negative results (19), nearly all of these negative biopsies have been BPH patients (26). Moreover, in order to differentiate between BPH and prostate cancer, two tactics are used. Typically, the degree of elevated PSA can predict which is the case. Men with a PSA between 2 and 10 generally have BPH, whereas men with PSAs above this level are more likely to have cancer (26, 32). Secondly, the free PSA test (fPSA) measures the % free (versus bound) PSA in the blood. Men with a higher fPSA are more likely to have BPH, whereas men with greater PSA binding (lower %fPSA) are more likely to present with prostate cancer. This exam, when used under suspicious PSA conditions vastly improves the ability to rule out prostate cancer and avoid unnecessary biopsies.

**PSA Era and Prostate Cancer History**

Since the introduction of the PSA exam in the late 1980s, history indicates that the national incidence of prostate cancer rose sharply during the early nineties of the PSA era, and fell just as abruptly, peaking in 1992 (14,15, 29,30,) with an incidence of 236.2/100,000 (29) (Fig. 1).

![Graph showing age-adjusted incidence per 100,000 of prostate cancer for the state of Utah, with peaks in 1992 and returning to pre-PSA era incidence.]

While these results have been perceived by the media (29) to indicate a decline in incidence, the cull phenomenon explains that in fact, the true incidence did not decline.
The essence of the cull phenomenon is that with the introduction of any successful screening method, and therefore increased screening, more people are being tested and the incidence appears to rise in the national population. This is depicted in the positive slope of Fig. 1. The second portion of the peak, with negative slope, depicts the result of increased screening and diagnosis. The apparent rapid decline in prostate cancer detection was due to the removal of detected people from the testable population. Since there were fewer cancerous people to test after 1992 (Fig. 1), the incidence appeared to decline, and the problem seemed solved, thus causing a decrease in testing frequency (8, 14).

Because AA men comprise only a small fraction of the men screened for prostate cancer, we question whether or not this reported cull phenomenon is representative of the AA community.

Perhaps limited access to medical care (such as PSA screening and follow up) among AA men has caused a delayed cull phenomenon in African American men, where this entire graph (Fig. 1) is right-shifted several years. This would explain the current discrepancy in PSA and cancer detection. Perhaps, for numerous reasons, not all African American men with prostate cancer have been removed from the population; and in capturing them now, their incidence and grade only appear to be greater than that of the rest of the population. Evidence supporting a potentially delayed cull phenomenon includes the percentage of PSA screening from race to race. A difference in AA and EA PSA exam usage over time has already been observed. Etzioni et al found that PSA use for white men stabilized at 35% in 1995 and has been relatively consistent through 1998
while the use of the PSA exam for black men was 31% in 1998 and was still increasing at that time (10).

If genetic differences were solely responsible for the discrepancy in prostate cancer incidence, we would expect that in comparison to Fig. 1, the incidence pattern of AA men would be shifted up the y axis. In comparing racial differences between factors like the grade of cancer, PSA and incidences of PIN and prostatitis over time, we would not expect to see a change in discrepancy. All changes would appear parallel if genetics were the only factor.

By potentially revealing that in fact African Americans are not bound to poor health by a “cancer gene” which more severely predisposes them to prostate cancer, or are no longer under-privileged in medical access as they may have been, it is possible to instill much hope to this community and further encourage them in their progressive health movements. Observation of a cull phenomenon would be indicative of such health improvement.

The goal of this retrospective research is to examine the PSA discrepancy in African American men compared to European American men in order to elucidate a cause for the existing disparities in prostate cancer incidence and grade and PSA scores. We postulate that as a result of limited access to health care, AA men have not experienced the cull phenomenon to the degree of EA men. In addition to the PSA exam and race, multiple parameters such as age; presence of prostatic inflammation (prostatitis), Prostate Intraepithelial Neoplasia (PIN), and cancer; and Gleason scores were statistically compared throughout the decade. By examining these factors via the medical charts of prostate biopsy patients from 1990-1991, 1999-2001, we were able to
include the properties of PSA history at this tertiary care center into our more thorough analysis of the observed African American PSA discrepancy.

Methods:

Prostate biopsy patients from a tertiary care center, The Cleveland Clinic Foundation’s Urological Institute, comprised the patient population of this retrospective study on the relationships between factors associated with prostate cancer. In addition to the 769 medical charts from 1999 – 2001 recalled from Lastword computerized chart software, 145 medical charts from 1990 and 1991 were requested since these years were among the peak years of prostate cancer diagnosis in the United States (15, 29, 30). Further, at this latter time, the PSA test was clearly a well accepted screening test for prostate cancer since being introduced in 1986. Therefore the comparison between these two time periods (90/91= Time 1 & 99-01= Time 2) enabled determination as to whether or not African American men were concurrently experiencing a major peak in incidence with the population in general.

Of the original time period examined, 1999-2001, the non-Caucasian category of men consisted of five men out of 143 that were not African American. Therefore these three Asian and two Hispanic men were removed from the study to eliminate variation in the comparison between races. Only African-American and European-American men were included in the study. In Time 1, there were 25 self-identified African American men and 120 European-American men. In Time 2, there were 138 and 631 self-identified African and European American men included respectively.
Multiple parameters were statistically examined throughout the study: age, race, prostate biopsy results, presence of prostatitis, presence of Prostatic Intraepithelial Neoplasia (PIN), and Gleason score in those with prostate cancer. Prostatitis is a pathological factor included in this study to counterbalance factors like age and race. Further, prostatitis is expected to be responsible for negative biopsies (19) and can be a factor elevating PSA (4). PIN is a pre-invasive growth in the prostate that inevitably results in prostate cancer. It is used as a highly predictive marker for prostate cancer. Gleason scores offer a quantitative analysis of cancerous cells depending on their similarity to normal cells. Moderately progressed cancer is most like the prostate and is considered “well differentiated”; this receives a score of between 1 and 4. More severe cases can receive scores of 5. Typically, the sum of two scores yields the overall Gleason score (for instance 3+4=7).

Initial comparisons of AA and EA and Time 1 and Time 2 were performed with nonparametric Wilcoxon rank-sum tests for continuous variables such as PSA and chi-square tests for binary variables such as whether or not a man had PIN (yes/no). Further, these analyses were performed to compare the two times and also to compare the cancer and non-cancer subgroups within each time. To determine the role of race and its interaction with other variables, multiple regression was used to determine which factors were significantly associated with PSA. Also, to determine the role of race and its interaction with other variables to predict cancer, multiple logistic regression was used. Due to the non-normal distribution of PSA, base-10 log of PSA was used in these analyses; however, all PSA scores have been translated back for the reader. All
calculations were performed using SAS version 8.1 software (SAS Institute Inc, Cary NC) and JMP.

**Results:**

In general the patient population grew over time from 145 in the early 90s to 769 at the end of the decade. However, within each decade, the percentage of blacks to the entire population remained rather consistent, (17.2%, 17.6%) for T1 and T2 respectively. Age within each population and race also did not change significantly.

<table>
<thead>
<tr>
<th></th>
<th>Time I n= 145</th>
<th>Time II n= 769</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>w=120 b=25</td>
<td>w= 631 b= 136</td>
</tr>
<tr>
<td>Mean Age</td>
<td>67.42 64.48</td>
<td>66.3 66.53</td>
</tr>
<tr>
<td>PSA log</td>
<td>1.67 2.25</td>
<td>1.95 2.3</td>
</tr>
<tr>
<td>PSA</td>
<td>6.49 9.58</td>
<td>7.02 10.91</td>
</tr>
<tr>
<td>Prostate Cancer</td>
<td>35% 60%</td>
<td>40% 49.60%</td>
</tr>
<tr>
<td>Gleason</td>
<td>6.15% 7.18%</td>
<td>6.52% 6.54%</td>
</tr>
<tr>
<td>PIN</td>
<td>5.90% 33%</td>
<td>42.30% 56.40%</td>
</tr>
<tr>
<td>Prostatitis</td>
<td>17.50% 12.50%</td>
<td>38% 33.80%</td>
</tr>
</tbody>
</table>

Table 1. Comparisons of data between race within each time period. In Time 1, Gleason score and %PIN were significantly higher among black men; and the percentage of men with positive biopsies for prostate cancer approached significance. In Time 2, PSA, incidence of prostate cancer, and incidence of PIN were significantly higher in black men.

<table>
<thead>
<tr>
<th></th>
<th>Race</th>
<th>Race and Time</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Time</td>
<td>Time and Time</td>
</tr>
<tr>
<td>PSA</td>
<td>0.0003</td>
<td>0.2811</td>
</tr>
<tr>
<td>Cancer</td>
<td>0.0055</td>
<td>0.8362</td>
</tr>
<tr>
<td>Gleason</td>
<td>0.0020</td>
<td>0.7140</td>
</tr>
<tr>
<td>PIN</td>
<td>&lt; .001</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Prostatitis</td>
<td>0.3664</td>
<td>0.0099</td>
</tr>
<tr>
<td>Age</td>
<td>0.2068</td>
<td>0.6254</td>
</tr>
</tbody>
</table>

Table 2: Because the goal of this thesis is to not only examine the racial differences in the parameters surrounding prostate cancer, but also the different ways these parameters in black and white men have changed over time, this table displays the resulting p-values
of three issues. The first column pools both times together, but only separates by race. The second column examines the entire biopsy population’s response to time. The third column, “Race and Time”, examines the interaction of these two variables. Statistical significance in the third column means that over time, each race changes differently.

<table>
<thead>
<tr>
<th></th>
<th>Time I Cancer</th>
<th></th>
<th>Time I Non-Cancer</th>
<th></th>
<th>Time II Cancer</th>
<th></th>
<th>Time II Non-Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>White</td>
<td>Black</td>
<td></td>
<td>White</td>
<td>Black</td>
<td></td>
<td>White</td>
</tr>
<tr>
<td></td>
<td>Mean</td>
<td>Std Dev</td>
<td>Median</td>
<td>Mean</td>
<td>Std Dev</td>
<td>Median</td>
<td>Mean</td>
</tr>
<tr>
<td>Age</td>
<td>68.31</td>
<td>8.01</td>
<td>70</td>
<td>65</td>
<td>10.38</td>
<td>64</td>
<td>66.87</td>
</tr>
<tr>
<td>PSA</td>
<td>12.06</td>
<td>3.25</td>
<td>11.58</td>
<td>21.98</td>
<td>4.37</td>
<td>32.46</td>
<td>4.57</td>
</tr>
<tr>
<td>Gleason</td>
<td>6.19</td>
<td>1.18</td>
<td>6</td>
<td>7.18</td>
<td>1.25</td>
<td>7</td>
<td>5.3</td>
</tr>
<tr>
<td>PIN</td>
<td>7.1</td>
<td>NA</td>
<td>NA</td>
<td>28.6</td>
<td>NA</td>
<td>NA</td>
<td>22</td>
</tr>
<tr>
<td>Prostatitis</td>
<td>9.5</td>
<td>NA</td>
<td>NA</td>
<td>7.14</td>
<td>NA</td>
<td>NA</td>
<td>20</td>
</tr>
</tbody>
</table>

Table 3. Comparison of cancerous and non-cancerous patients over time divided by race.

**PSA**

PSA did differ significantly by race (p=.003) (Table 2). Within T1, the racial difference between PSA was not significant (p=.19) (Table 1). Within T2, the mean PSA of black men, 10.91, was significantly greater than the mean PSA of white men, 7.02 (p=.001) (Table 1). When the entire population was divided only by time, PSA did not differ by time (p=.2811) (Table 2). There was not an interaction between time and race.
We separated patients between cancerous and non-cancerous patients to more closely examine PSA (Fig. 3). Upon subdividing each time and race into cancerous and non-cancerous subgroups (Fig. 3), it is abundantly evident that this racial disparity in PSA is particularly due to the presence of cancer ($p=.0235$). The black and white non-cancerous patients present virtually the same PSA elevation over time. However, the PSA of black cancerous men (21.91 and 12.94 for T1 and T2) is greater than that of white cancerous men (12.02 and 7.96). According to Table 3, this difference is not statistically different.

Prostate cancer

Cancer differed only by race, where the average incidence of cancer pooled over both times was greater in AA (52%) than EA (39%) men ($p=.0055$) (Fig. 4). This racial disparity existed in both times (Table 1). The greater incidence of prostate cancer among AA men in the early 90s (60% vs 35% in EA men) approached significance ($p=.06$) (Table 1). By the end of the decade, this greater incidence (49.60% vs 40% respectively) was statistically significant ($p=.04$) (Table 1) due to a larger patient population. However, when races were pooled and only divided by time, cancer incidence did not change ($p=.8362$) and the response to time did not vary by race ($p=.3006$) (Table 2).
Fig. 4 When times were pooled, the average incidence of cancer among black men was 52%, while it was 39% for white men. This difference is significantly different (p=.0055).

**Gleason Score**

When T1 and T2 were pooled for each separate race, there was an overall racial difference in Gleason scores. Black men tended to have greater Gleason scores, a more severe form of cancer, than white men (p=.002) (Table 2). Further, there was a racial difference in Gleason scores over time, meaning that over time, each race’s grade of cancer changed differently (Fig. 5). The racial disparity in Gleason scores is supported by T1 (p=.02) results (Table 1); however, by Time 2, there was hardly a difference in Gleason scores (p=.9) (Table 1).

Gleason scores decreased for black men, but increased for white men. While a significant difference in Gleason scores existed in the early 90s, Gleason scores were virtually identical in T2 because the grade of cancer decreased for black men (7.18 → 6.66), yet increased for white men (6.15 → 6.53) (Fig. 5).
Fig. 5 The interaction between time and race observed in Table 2 is expressed in the differences in slopes seen here. Over time, the change in Gleason score varies by race.

**PIN**

In general, more black men presented with PIN than white men (p < .001) (Table 2). This is corroborated within our study by significant results of both Times 1 and 2. In Time 1, 33% of black men had PIN while only 5.9% of white men presented with PIN (p = .002) (Table 1). In Time 2, 56.4% and 42.30% of black and white men respectively presented with PIN (p = .003) (Table 1). Over time, when both races are pooled together, PIN changed significantly (p < .001) (Table 2). In fact, it appears that there was an interaction between these two factors, race and time (p = .0127), meaning that the effect of time depends on race (Fig. 6). When we subdivided into cancerous and non-cancerous subgroups, even non-cancerous black men presented with PIN significantly more often (Table 3).
Prostatitis

Prostatitis does not significantly change between race, although it appears that EA biopsy patients have prostatitis more often than AA men (17.5% and 12.5%, 38% and 33.8%) for EA and AA men of T1 and T2 respectively (Table 1). Since European American men also have prostate cancer less frequently than African Americans, it appears that there may be a negative correlation between prostatitis and prostate cancer. The only significant change was an increase in incidence of prostatitis over time (p = .0099) (Table 2) (Fig 7). There was not a racial temporal interaction regarding prostatitis.

Age

Age never appeared to change, whether between races (p = .68 for T, p = .37 for T2) p = .2068 for pooled times Tables 1,2), or over time (p = .6254).

Discussion:

The unchanging percentage of African Americans in our test population (~17%) suggests one of two possibilities. It is possible that the Cleveland Clinic has made a more concerted effort to reach African American communities within Cleveland. This lack of change also may indicate that we are consistent in continuing the effort to maintain contact with the African Americans which comprise 18% of the Cleveland population.
Consistent age indicated that condition at the time of biopsy was not age-related. This means that the two races were equally compared with respect to age and that the reported differences in PSA, cancer incidence, Gleason score, PIN and Prostatitis are not due to age. Similar ages throughout race and time indicate no genetic differences or improvement in limited access.

Regarding the differences reported in our study, it could be the case that in order to treat AA men earlier in the process of progression, they may need more specific care earlier in life. Whittemore and Cooney found that AA men naturally have higher PSA than white men and found it unnecessary to subdivide for age between races when screening for prostate cancer (35, 9). It has also been reported that AA men had higher baseline serum PSA levels at the early ages between 20 and 45 years of age compared to EA men (22). The physiological significance of those results was and has not been determined.

Over time, the PSA of black cancerous men improved greatly, which supports our postulation that the racial PSA difference was magnified by limited access, and that much is successfully being done in the Cleveland area to combat this. Since the non-cancerous PSA among European and African Americans is virtually the same (Fig. 3) and the only major PSA difference exists in cancerous men, it appears that the reason a PSA difference occurs in the first place is in part due to the presence of prostate cancer. Powell et al also observed decreased PSA over time and assert that if genetics is responsible for PSA differences, that genetic differences are associated with cancer only (21). The lack of significance that we measured in PSA of cancerous AA and EA men \( p = .14 \) is most likely due to the small patient population of Time 1.
The positive predictability of the PSA test may not be consistent throughout race. Therefore, the rate of change of PSA has been examined by Carter et al to conclude that it may enhance the sensitivity and specificity of PSA’s prostate cancer prediction (7) from race to race. Stephenson et al in 2002 supplemented PSA rate of change studies with their conclusion that a strong correlation with disease progression exists when PSA doubles in less than or equal to 120 months (28).

The main issue with respect to our prostate cancer results addresses the confounding results in T2, where the actual differences in incidence are more converging (Table 1), but their difference gains statistical significance (from .06 to .04 over time). We attribute this to patient population.

Actually, along with decreased incidence within the AA population and decreased PSA in cancerous men, decreased Gleason scores also contradicted our hypothesis that neither genetic differences or a delayed cull phenomenon is the reason for racial differences. If genetic differences were the case, again, no convergence should be observed. If a delayed cull phenomenon were the case, we would expect that incidence and grade of cancer and PSA would all diverge from those statistics of European American men. Instead, our studies find that they converge with EA statistics and improve by decreasing. This suggests that in fact, the proposed cull phenomenon for the nation primarily comprised of EA men actually does also represent AA men over time.

Further, in order for such improvements to be made, we suggest that increased awareness on behalf of both doctors and patients has enabled tighter vigilance of AA men.

However, it was surprising to find that age did not change over time considering the decreased grade of cancer in AA men. We would expect age to decrease in order to
capture at earlier ages. Our lack of racial difference in age contradicts Whittemore who found that AAs present cancer at the age of 66.8 years, not 72.5 years like EA men (35).

To simply biopsy in every instance of elevated PSA, as a practice of tighter vigilance, is not entirely necessary. It does no good to biopsy a man whose elevated PSA is due to other circumstances such as prostatitis or BPH. Further, there are risks entailed in a biopsy and the procedure is relatively expensive. Common PSA scores of BPH are between 2 and 10; and there is a weak relationship between these PSAs and prostate cancer (26). Thus, in examination of Figure 3, the non-cancerous patients are all relatively similar in PSA values over time (~3 ⇒ ~ 7 for T I and TII). These PSA values are comparable to BPH and it is most likely that these people are progressing towards prostate cancer or that they present BPH since BPH is the most common diagnosis in the event that cancer is not present (26 and 34). Further, prostatitis has been found to elevate PSA (4, 32) and chronic prostatitis is clearly linked with BPH (4, 32). Therefore, it has been recommended that prostatitis detection precede prostate biopsies in order to decrease the occurrence of negative biopsies (4,19). These past conclusions seem to be supported by our findings that prostatitis may predict a decreased likelihood of prostate cancer. We continue to encourage the use of such pathological factors to supplement PSA screening and enhance positive prediction.

Limitations

This study offers a wide variety of information for future study from more thoroughly tracing the cull phenomenon to pathological research regarding prostatitis. However, several limitations to our study should be realized when consulting this paper and comparing it to the research of other scientists. The low number of African
American men in the population of Time 1 may have skewed the data and the ability to determine significance in differences such as the PSA differences of cancerous men of Time 1.

Secondly, the results in Figure 4 must be clarified given the temporal context of PIN. While PIN is now commonly used, it was used irregularly in 1990 and 1991. Thus, the incidence of PIN in Time 1 appears lower than actuality because not all men were tested for PIN. While we cannot consider the temporal difference in PIN observed in this study valid, the racial differences in PIN do reflect reality, as this difference existed in the more reliable Time 2.

Although the mildly inconsistent screening of PIN may be a limitation of this experiment, the study of PIN does deserve significant future attention. In Time 2, PIN was only significantly different in non-cancerous patients, and oddly not among cancerous patients (Table 3). Since this cannot be explained, future study would be crucial especially considering that PIN in the premalignant stage must progress to adenocarcinoma.

A limitation common to any scientific experiment is that the Cleveland Clinic representation of access to health care solely within Cleveland is only a very small sample of the national population. Since 60% of white men and 70% of black men at risk for prostate cancer are not being screened (10), we do not know if the results of our study, specifically those of AA men, are consistent with the traits of many unscreened men.

Finally, to more confidently determine whether or not a delayed cull phenomenon is at all possible, data from each year of the decade is necessary.
Conclusions:

We attempted to determine whether or not the asserted cull phenomenon represented the AA population as well as the rest of the national population, and/or whether a potentially delayed cull phenomenon explained increased AA PSA scores and increased incidence and grade of cancer. Our improving and converging results with those of EA men lead us to believe that the cull phenomenon does represent AA men, rather than a delayed cull phenomenon or any other pattern being more representative. In fact, because our results converge, they suggest that the differences that AA and EA men present upon the time of biopsy are not entirely due to genetic factors. It appears that the AA improvements over time suggest that improved access and greater awareness play a significant role in narrowing the gap.
Author's Note:

Given the small amount of knowledge acquired throughout the research of this topic, I plan to continue encouraging black men and their primary care physicians to value PSA testing. While not all primary care physicians value the PSA test for its cost and flaws, this test clearly aids tertiary care physicians in monitoring the progression of disease. Establishing a solid base line throughout one’s lifetime enables better interpretation of PSA scores nearing the threshold of 4. As the different levels of care within a medical community act as a team, communication between these levels of care is vital for health improvements.

The fear of cancer should not deter people from taking preventative or early action measures. It is actually more cost effective than handling cancer at progressed stages. But more significantly, when a person chooses medical action over avoiding the mental stress associated with bad news, the quality of life is preserved to a greater degree because a person can avoid enduring the even greater stresses of intense cancer.

My hope is that all people would not waste precious life by letting something treatable (and to some degrees preventable) like cancer fester. I hope and pray that people would be equipped with the knowledge that would allow them to take the focus off of health and on to more important things such as the love for their families, friends, and people they do not even know. The reason why I have appreciated this study is because I enjoy serving people in this way so that they may better experience the abundance that life offers. Life is too sweet to sit on the sidelines. C.S. Lewis best embodies my ultimate goal and challenge for every person I encounter, including myself, “We are… like an ignorant child who wants to go on making mud pies in a slum because he cannot imagine what is meant by the offer of a Holiday at the sea. We are far too easily pleased.”
Citations


