Re: Race, Prostate Cancer Survival, and Membership in a Large Health Maintenance Organization

We believe that the article by Robbins et al. (1) was generated with good intentions; however, this study does a disservice in improving our understanding of the relationship between prostate cancer and race. The authors made numerous assumptions that require commentary.

First, cancer researchers do not decide that hormonal therapy or chemotherapy prolongs survival in prostate cancer, breast cancer, or any other cancer on the basis of large population-based studies (2). The U.S. Food and Drug Administration approval for the use of a new drug is not based on large, crude, population-based studies. If the sample size for these studies is adequate to show small treatment effects as independent prognostic factors, they should be large enough to detect a meaningful independent effect due to race. The use of large numbers of patients does increase the statistical power, but it also increases the risk that if there are differences in the incidence of screening, work-up, quality of care received, support systems, or other socioeconomic factors (not included in the analysis), then the conclusions are likely to be in error. Instead, we conduct carefully designed prospective randomized trials with well-defined stratified risk groups of patients who are systematically and uniformly staged, treated, and followed to eliminate various sources of potential biases.

The article by Robbins et al. (1) contributed little new information. Studies (3,4) based on crude, population-based data have demonstrated that blacks present with more advanced prostate cancer. The suggestion that their report was unique because it involved a putative “equal access” health maintenance organization is overrated. They assumed that health plan members all utilize health care equally. They provided no data to support this assertion. In fact, numerous studies have demonstrated that blacks are treated differently than whites. For example, with the same severity of heart disease, whites are more likely to receive cardiac catheterization than blacks (5). The point is that equal access does not equate to uniform treatment, and there are known examples of differences in treatment by race (5,6).

It is an error to group patients into broad staging categories called “local” and “regional” and assume that there are no important differences in outcome. The extent of disease and the corresponding prognosis associated with particular cancers are actually continuous and not simply discrete units of prognosis. Numerous studies have demonstrated that clinical stage is a crude measure of the true extent of disease in prostate cancer. A major flaw in this study was to group clinical patients with stage C disease and patients with known lymph node metastasis; such patients have quite different prognoses. No modern randomized trial would stratify only on the basis of stage. Pretreatment prostate-specific antigen and Gleason scores are the major determinants of pathologic stage and ultimately the outcome in patients with clinical, localized prostate cancer.

These authors assume that tumor grade should not be accounted for in the analysis of race. Tumor grade increases with stage and as such, is not likely to be independent to the time of diagnosis. The question should not be, “if a black person presents with a higher stage and grade tumor and they are treated differently, are they more likely to die of it?” The question should be, “if a black person presents with the same grade and stage and gets the same treatment, are they more likely to die of it due to this concept that we call ‘race’?” Furthermore, the distribution pattern differences noted between blacks and whites with prostate cancer are not unique to prostate cancer. The stage at presentation for blacks is higher for most cancers, including cancers of the breast, lung, and esophagus. For all of these sites, analysis of prospective randomized trials have demonstrated that race has no independent effect.

In this article, the authors conclude that there is an increased virulence of prostate cancer in black men. However, in an earlier study, Whittemore et al. (7) showed that there was no difference in the rate of rise of prostate-specific antigen levels by race in a longitudinal study. This lack of difference suggests that there is likely to be no difference in virulence over time. An even more convincing argument against the conclusions of these authors is provided by their own data [see (1), Table 1]. If the difference between the stage and tumor grade among blacks and whites within the Kaiser system is explained by biologic differences, the same argument could be made comparing whites within the Kaiser system to non-Kaiser whites (Table 1).

Comparison of Kaiser members versus non-Kaiser members*

<table>
<thead>
<tr>
<th>Stage</th>
<th>Kaiser member</th>
<th>Non-Kaiser subject</th>
</tr>
</thead>
<tbody>
<tr>
<td>Localized</td>
<td>62.6</td>
<td>55.2</td>
</tr>
<tr>
<td>Regional</td>
<td>16.7</td>
<td>17.3</td>
</tr>
<tr>
<td>Distant</td>
<td>15.7</td>
<td>21.9</td>
</tr>
</tbody>
</table>

*Robbins et al., 1998 (1).
construct, we would take issue with this conclusion.

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RESPONSE

We appreciate the interest of Roach et al. in our analysis of survival among black and white prostate cancer patients in the San Francisco Bay Area (1). The investigators have raised important issues, and we welcome the opportunity to respond to them. They argue against biologic factors as an explanation for poorer stage-specific survival of black prostate cancer patients compared with white patients. Instead, they argue that the observed higher death rates in blacks can be explained completely by racial differences in socioeconomic barriers, such as inadequate access to health care, to good treatment, and to health education leading to earlier diagnosis. We would like to believe this argument because it means that preventive strategies could eliminate the observed survival differences. Unfortunately, however, it is not supported by the data we analyzed.

The hypothesis that the black survival disadvantage can be explained completely by socioeconomic barriers predicts that the disadvantage is decreased when some of these barriers are removed. Since financial access to medical care is an important barrier that is eliminated in a health maintenance organization (HMO) such as the Kaiser Permanente Medical Care Program (KPMCP), the hypothesis predicts a smaller survival disadvantage for black KPMCP members than for black nonmembers. In contrast, the data showed similar stage-adjusted black/white death rate ratios of 1.28 for KPMCP members and 1.22 for KPMCP nonmembers. Thus, the data do not support the hypothesis.

Roach et al. fault us for not adjusting our analysis for tumor grade. Requiring that two patients (one black and one white) have tumors with the same grade puts them on artificially equal footing with respect to an important indicator of tumor aggressiveness. If black men have poorer survival because their tumors are more aggressive, adjusting for grade will mislead us into believing that eliminating all socioeconomic barriers will eliminate all survival differences. The question we raised was “Can the poorer stage-specific survival of blacks compared to whites be explained by differences in access to medical care, or is it due at least in part to biologic differences in tumor characteristics?”

To support their argument that black versus white survival differences are unrelated to black versus white tumor characteristics, Roach et al. cite data from KPMCP prostate cancer patients showing no black versus white differences in prediagnostic prostate-specific antigen measurements (2). However, these measurements were taken many years before diagnosis and so do not pertain to tumor characteristics or survival. In contrast, Roach et al. fail to cite data from an equal health care setting showing substantial differences in tumor features between black and white patients (3). They also fail to cite autopsy data suggesting that prostate cancers in blacks are more aggressive than those in whites of the same age (4,5). It is difficult to explain the autopsy findings on the basis of racial differences in socioeconomic factors.

Roach et al. criticize us for failing to comment on randomized trials that show similar survival for blacks and whites, citing a paper by Bolla et al. (6). It is not clear why this paper is relevant, because it does not mention the participants’ ethnicities. Roach et al. argue that randomized trials are superior to population-based data, because the latter do not control adequately for confounding factors. Yet, the strengths of randomized trials stem from their freedom from confounding with respect to comparison of the treatment arms under study and not from confounding with respect to comparisons of auxiliary, nonrandomized variables, such as ethnicity. Moreover, the participants in these trials may have been selected for factors related to prognosis, limiting generalization of ethnic comparisons to more general populations.

Roach et al. also mistake our conclusion as being genetically based. Although there may indeed be genetic factors involved, we also believe that nongenetic factors, for example, diet or exercise, may influence tumor aggressiveness.

Roach et al. accuse us of assuming that all HMO members utilize health care equally. Yet, we clearly stated: “Systematic racial differences in survival within stages could plausibly arise, even in equal health care systems, if there were important racial differences in factors such as frequency of contact with health care providers. An important point is that equal-access health care systems can only guarantee equality of covered benefits for enrolled members, not equality in the frequency of use of all forms of care.” Roach et al. also state that we did not address the possibility of residual confounding by stage. Yet we clearly acknowledged “...within each of the three broader Surveillance, Epidemiology, and End Results (SEER) stages used in the present study, racial differences in survival still could exist if white men in a given stage were diagnosed on average at an earlier point in the history of their cancers.”

Roach et al. complain that we do not attribute survival differences between
whites in and out of the KPMCP to biologic factors. But comparing black versus white survival among men with uniform financial access to care is quite different from comparing survival of whites with unequal financial access. It is precisely this distinction between an ethnic comparison within HMO members and a member versus nonmember comparison within ethnic groups that motivated our analysis.

Roach et al. compare our analysis to the infamous Tuskegee syphilis trials and cite their earlier conclusion that any interpretation of the observed black versus white survival differences as due to biologic factors is “racist” (7). We believe that such a conclusion, a priori of a full evaluation of the data, constrains studies to be politically correct and does a disservice to the scientific community and the public. Indeed, any restraints on objective analysis of data do a disservice to all prostate cancer patients.

In conclusion, we agree with Roach et al. that much of the survival disadvantage of black men may be due to their disproportionate burden of barriers to the best health care. We need to address these inequities. However, the data suggest that some of the disadvantage may also be due to biologic differences in tumor characteristics. We believe to dismiss this possibility would be a disservice to good science and the community.

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