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Differences in vitamin D status may account for unexplained disparities in cancer survival rates between African and white Americans

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Considerable disparities in cancer survival rates exist between African Americans (AAs) and white Americans (WAs). Various factors such as differences in socioeconomic status (SES), cancer stage at time of diagnosis, and treatment—which this analysis considers primary explanatory factors—have accounted for many of these differences. An additional factor not usually considered is vitamin D. Previous studies have inversely correlated higher solar ultraviolet-B (UVB) doses and serum 25-hydroxyvitamin D (25(OH)D) concentrations with incidence and/or mortality rates for about 20 types of cancer and improved survival rates for eight types of cancer. Because of darker skin pigmentation, AAs have 40% lower serum 25(OH)D concentrations than WAs. This study reviews the literature on disparities in cancer survival between AAs and WAs. The journal literature indicates that there are disparities for 13 types of cancer after consideration of SES, stage at diagnosis and treatment: bladder, breast, colon, endometrial, lung, ovarian, pancreatic, prostate, rectal, testicular, and vaginal cancer; Hodgkin lymphoma and melanoma. Solar UVB doses and/or serum 25(OH)D concentrations have been reported inversely correlated with incidence and/or mortality rates for all of these cancers. This finding suggests that future studies should consider serum 25(OH)D concentrations in addressing cancer survival disparities through both measurements of serum 25(OH)D concentrations and increasing serum 25(OH)D concentrations of those diagnosed with cancer, leading to improved survival rates and reduced disparities.

Background

Considerable disparities in cancer survival rates exist between African Americans (AAs) and white Americans (WAs). Various factors such as socioeconomic status (SES),[1] cancer stage at time of diagnosis, and treatment[2] have accounted for many of these disparities. Educational attainment is often used as a proxy for SES.[3] Other factors include insurance status,[4] social determinants in general[5,6] and genetics.[7,8] However, even when analyses of cancer survival data include all known or suspected factors affecting survival, AAs still tend to have a lower survival rate than that of WAs, possibly because of unmodeled factors such as biological differences, and perhaps as a consequence of educational level and access to health care as several authors have noted.[9-12]

Discussions of cancer survival disparities generally overlook the role of vitamin D. For 2001–2004, AAs older than 60 y had a population mean serum 25-hydroxyvitamin D [25(OH)D] concentration of 17 ng/ml compared with 25 ng/ml for WAs.[13] Prevalence of hypovitaminosis D [(25(OH)D $<$ 15 ng/ml] in the South was 45% among blacks and 11% among whites.[14] In patients participating in a randomized controlled trial of chemotherapy, serum 25(OH)D concentrations were lower in black patients than in white patients and patients of other race (median, 10.7 vs 21.1 vs. 19.3 ng/ml, respectively; $p < 0.001$), as well as in females compared with males (median, 18.3 vs 21.7 ng/ml, respectively; $p = 0.0005$).[15] Solar ultraviolet-B (UVB) irradiance is the primary source of vitamin D for most Americans, accounting for 80–90% of vitamin D.[16] AAs, with darker skin, are less efficient at producing vitamin D from UVB irradiance.[17] In addition, AAs are less likely to have as much vitamin D from oral intake.[18]

A large body of literature supports a beneficial effect of vitamin D in reducing the risk of cancer incidence and mortality rates. The UVB-vitamin D-cancer hypothesis was proposed in 1980.[19] Many ecological studies[20-24] have supported this hypothesis, as have observational studies of breast and colorectal cancer.[25,26] Two ecological studies found stronger inverse correlations between solar UVB doses and cancer mortality rates than incidence rates.[23,24] Several reviews of the UVB-vitamin D-cancer hypothesis have also been published.[27,28] Two randomized controlled trials found positive effects.[29,30]

The dose–response relation for vitamin D has been derived from observational studies for breast and colorectal cancer.[25] For the differences in population mean serum 25(OH)D concentrations for 2001–2004,[13] the dose–response relations for breast and colorectal cancer indicate a 20–25% increase in incidence rate. The values for cancer incidence are not necessarily the same for cancer survival, but they do suggest the magnitude of the effect. This vitamin D-cancer dose–response relation might underestimate the effect of lower serum 25(OH)D concentrations

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for AAs since 20% of the black population is older than 60 y, in contrast to only 6% of whites; also, the risk of cancer increases more rapidly for changes of serum 25(OH)D concentration at lower concentrations.

A recent paper addressed vitamin D's role in explaining some of the cancer survival disparities. Data from the Third National Health and Nutrition Examination Survey (NHANES III) were used to investigate the role of racial disparity from colorectal cancer; adding vitamin D deficiency to the model attenuated the mortality risk associated with being black by a statistically significant 40%.[31] Grant and Peiris[32] investigated vitamin D's role in explaining disease disparities between AAs and WAs in general.

This paper surveys the literature on cancer disparities for AAs and WAs as well as the literature on epidemiological studies on vitamin D and cancer to see whether differences in serum 25(OH)D concentrations might explain many of the otherwise-unaccounted-for residual disparities.

Results

Table 1 presents the findings regarding cancer survival with respect to serum 25(OH)D concentrations at the time of diagnosis. Significant inverse correlations between 25(OH)D and cancer survival were found for all-cancer, breast, colon, colorectal, lung,

Table 1. Evidence that vitamin D increases cancer-specific and all-cause survival rates

Cancer type	Conditions	Recurrence, vitamin D deficiency [HR (95% CI)]	Survival, vitamin D adequacy [HR or RR (95% CI)]	Survival, vitamin D deficiency [HR or RR (95% CI)]	Reference
All	Vitamin D supplementation in intention-to-treat		HR = 0.85 (0.68–1.06) (mortality)		33
All	Norway, 9.3-y follow up, high vs. low quartile		HR 0.36 (0.27–0.51) $p < 0.01$ CS		34
Bladder	Three years of follow up, summer vs. winter diagnosis		RR = 1.0 (0.97–1.07) AC		35
Breast	Three years of follow up, fall vs. winter diagnosis		0.70 (0.65–0.75)		36
Breast	Three years of follow up, summer vs. winter diagnosis		RR = 0.75 (0.72–0.79) AC		37
Breast	Women in Canada, 11.6 y follow-up,	HR = 1.71 (1.02–2.86) for distant recurrence;		HR = 1.60 (0.96–2.64) AC	38
Breast, luminal	40-mo follow up	HR = 3.97 (1.77–8.91, p = 0.001)			39
Breast	Continuous per 10 nmol/L decrement; distant disease, overall mortality	HR = 1.14 (1.05–1.24) p = 0.006		HR = 1.08 (1.00–1.17) p = 0.07	40
Breast	Norway, 9.3-y follow up, high vs. low quartile		HR = 0.42 (0.21–0.82), p = 0.01 CS		34
Chronic lymphocytic leukemia, chronic lymphocytic lymphoma	Mean follow-up 36 mo (1–86 mo)	HR = 1.47 (1.11–1.96) p = 0.008		HR = 1.47 (0.97–2.23) p = 0.07 AC	41
Colon	Three years of follow up, fall vs. winter diagnosis		0.71 (0.66–0.77) men; 0.68 (0.64–0.72) women		35
Colon	Three-year follow up, summer vs. winter diagnosis, Midwest region, Norway		Men < 65 y, RR = 0.70 (0.5–0.83) AC Women < 65 y, RR = 0.77 (0.66–0.90) AC		42
Colon	Norway, 9.3-y follow up, high vs. low quartile		HR = 0.20 (0.01–1.10), p = 0.16 CS		34
Colorectal	Mean follow-up time 116 mo, used predicted 25(OH)D concentration		HR = 0.50 (0.26–0.95) CS		43
Hodgkin lymphoma	18 and 36 mo follow up, based on season, autumn vs. winter diagnosis, Norway		RR = 0.78 (0.62–0.99) p = 0.04 AC		44
Lung	Three years of follow up, summer vs. winter diagnosis		RR = 1.00 (0.98–1.02) AC		45
Lung	> 27.7 ng/ml vs. < 12.6 ng/ml		1.08 (0.75–1.57) p = 0.76 AC		46

Table 1. Evidence that vitamin D increases cancer-specific and all-cause survival rates (continued)

Cancer type	Conditions	Recurrence, vitamin D deficiency [HR (95% CI)]	Survival, vitamin D adequacy [HR or RR (95% CI)]	Survival, vitamin D deficiency [HR or RR (95% CI)]	Reference
Lung	Norway, 9.3-y follow up, high vs. low quartile		0.18 (0.11–0.29), $p < 0.001$, CS		34
Lymphoma	Norway, 9.3-y follow up, high vs. low quartile		HR = 0.39 (0.18–0.83), p = 0.01 CS		34
NHL, diffuse large B-cell lymphoma	5-y follow up	HR = 1.41 (0.98–2.04)		HR, 1.99 (1.27–3.13), AC	47
NHL, T-cell lymphoma	5-y follow up	HR = 1.94 (1.04–3.61)		HR, 2.38 (1.04–5.41)	47
Ovarian	Three years of follow up, summer vs. winter diagnosis		RR = 1.00 (0.98–1.07) AC		35
Prostate	Three years of follow up, fall vs. winter diagnosis		0.70 (0.66–0.74)		36
Prostate	Three years of follow up, summer vs. winter diagnosis		RR = 0.76 (0.73–0.79) AC		48
Prostate	The mean age (standard deviation, SD) at blood draw of participants in the analysis was 63.7 (7.8) years in HPFS and 59.2 (7.6) years in PHS. The mean age (SD) at cancer diagnosis was 69.5 (7.4) years in HPFS and 67.8 (6.5) years in PHS.			HR: 1.59 (1.06–2.39) P (trend) = 0.006 (lowest vs. highest quartile)	49

AC, all cause; CS, cancer specific; HR, hazard ratio; NHL, non-Hodgkin lymphoma; RR, relative risk.

prostate cancer, chronic lymphocytic leukemia/chronic lyphocytic lymphoma, Hodgkin lymphoma, and non-Hodgkin lymphoma. Studies also reported no significant correlation between serum 25(OH)D and survival for bladder, lung and ovarian cancer.

Table 2 presents the multifactor-adjusted hazard ratios for survival for AAs vs. WAs for cancer-specific survival. Inclusion of SES, stage at diagnosis, and treatment in the analyses is indicated. **Table 2** lists nearly all the relevant papers. The results for cancer-specific survival rates are a stronger indication of the effects of vitamin D than are all-cause survival rates because some of the all-cause deaths could be due to non-vitamin D-related diseases or to factors such as smoking. Statistically significant disparities emerged for cancer-specific survival rates for 13 types of cancer: bladder, breast, colon, endometrial, lung (non-small cell, stage III, IV), ovarian (advanced), pancreatic, prostate, rectal, testicular, vaginal cancer, Hodgkin lymphoma, stage II and melanoma. Our analysis also found statistically significant disparities for cancer-specific survival rates for two types of cancer, endometrial and ovarian cancer. There were no statistically significant findings for gastric adenocarcinoma, or head and neck, and oral cancer and leukemia.

Discussion

This review offers evidence to explain cancer survival differences between AAs and WAs. AAs' lower serum 25(OH)D concentrations (mainly from reduced vitamin D photoproduction owing to darker pigmentation) may account for much of the unexplained survival disparity after consideration of such factors as SES, stage at diagnosis, and treatment. All cancers for which a disparity in cancer-specific survival was reported also have evidence for a beneficial role of vitamin D, as do most of those for which we found disparities for all-cause survival.

One reason ecological studies are strong include that vitamin D plays an important role in reducing risk of cancer initiation and angiogenesis around tumors and metastases.[84,85] Since cancer can take years to decades to reach the stage of detection or death, continued high serum 25(OH)D concentrations over much of the lifetime is required for greatest risk reduction. Most recent ecological studies include various cancer risk-modifying factors in the analysis.[20-24] Also, ecological studies include many cases, thereby reducing the uncertainty of the values. Among 45-y-old British citizens, casual solar UVB irradiance in summer increased serum 25(OH)D concentrations by about 15 ng/ml,[86] enough to have an important impact on cancer risk.[25,29] For example, breast cancer incidence rates are highest in spring and fall.[87] The reasons for the seasonal variations given were increased production of vitamin D in summer and melatonin in winter. Breast cancer has several subtypes, and rate of progression can vary widely, with some being very rapid. For slower growing cancers, serum 25(OH)D concentrations in summer may be sufficient to retard or reverse the growth.

Once cancer reaches the point where it can be diagnosed, vitamin D improves cancer-specific survival by several mechanisms, including antiangiogenesis and antimetastases.[84,85] The disparities for hematopoietic cancers may be weak or nonexistent because angiogenesis and metastases are less important for blood cell-related tumors than for solid tumors. Higher serum 25(OH)D concentrations also affect all-cause mortality rates[88] since vitamin D protects against several major life-threatening

Table 2. Cancer-specific mortality rate disparities for AAs vs. WAs not explained by known factors for 25 types of cancer. Studies reported that AAs have significantly increased risk for 13 types of cancer after consideration of SES, cancer stage at time of diagnosis, and treatment

Cancer	SES	Cancer stage at diagnosis	Treatment	Relative Risk (95% CI), AAs vs. WAs	Ref.
Bladder		Y		1.68 (1.28–2.21)	50
Bladder, males, 1- to 2-y follow-up	Y	Y		1.26 (1.15–1.37)	12
Bladder, males, 3- to 4-y follow-up	Y	Y		1.16 (0.96–1.41)	12
Bladder, females, 1- to 2-y follow-up	Y	Y		1.20 (1.09–1.32)	12
Bladder, males, 3- to 4-y follow-up	Y	Y		1.55 (1.21–1.98)	12
Bladder	Y	Y	Y	1.73 (1.23–2.43)	51
Bladder	Y	Y	Y	1.29 (1.24–1.36)	52
Breast, meta-analysis	Y			1.23 (1.05–1.20)	53
Breast, meta-analysis		Y		1.22 (1.10–1.37)	50
Breast—premenopausal	Y	Y	Y	1.41 (1.09–1.84)	10
Breast—postmenopausal	Y	Y	Y	1.39 (1.17–1.66)	10
Breast, Stage 1, 2	Y	Y	Y	1.55 (1.13–2.13)	54
Breast (metastasis)	Y	Y	Y	1.20 (0.96–1.50)	55
Breast	Y	Y	Y	2.41 (1.21–4.79)	56
Cervical				No difference	57
Colon, meta-analysis	Y		Y	1.13 (1.01–1.28)	58
Colon		Y		1.19 (1.14–1.25)	59
Colon		Y	Y	1.15 (1.10–1.20)	59
Colon	Y	Y	Y	1.08 (1.03–1.13)	59
Colon, early stage	Y	Y	Y	0.99 (0.67–1.45)	10
Colorectal				1.33 (1.30–1.36)	60
Colorectal	Y	Y	Y	1.31 (1.21–1.42)	61
Endometrial		Y		2.08 (1.34–3.21)	50
Endometrial	Y	Y	Y	1.51	62
Endometrial		Y		1.60 (1.51–1.69)	63
Esophageal	Y	Y	Y	1.02	64
Gastric adenocarcinoma		Y	Y	1.03 (0.95–1.12)	65
Gastric adenocarcinoma			Y	1.18 (0.94–1.49)	66
Head and neck	Y	Y	Y	1.06 (0.50–2.25)	67
Hodgkin lymphoma, stage I	Y	Y		1.22 (0.81–1.85)	68
Hodgkin lymphoma, stage II	Y	Y		1.35 (1.12–1.62)	68
Leukemia, acute myelogenous	Y	Y	Y	1.05 (0.83–1.33)	10
Lung cancer, small cell, limited				1.11 (0.77–1.60)	10
Lung cancer, NSC, advanced				0.89 (0.75–1.05)	10
Lung cancer, NSC, stage I, II	Y		Y	0.97 (0.85–1.10)	69
Lung cancer, NSC, stage III, IV	Y		Y	1.24 (1.01–1.53)	69
Melanoma	Y	Y	Y	HR, 1.60 (1.17 –2.18)	9
Multiple myeloma	Y	Y	Y	0.85 (0.70–1.03)	10
Nasopharyngeal				1.00 (0.82, 1.24)	70
Non-Hodgkin's lymphoma (NHL)	Y	Y	Y	1.07 (0.92–1.25)	71
NHL, advanced	Y	Y	Y	1.17 (0.94–1.45)	10
Oral	Y	Y	Y	1.1 (0.9–1.4)	72
Ovarian, advanced	Y	Y	Y	1.41 (1.03–2.11)	10
Ovarian, stage 3		Y	Y	1.06 (0.61–1.79).	73
Ovarian, 1973–2007		Y	Y	1.14 (1.07–1.21)	74

Table 2. Cancer-specific mortality rate disparities for AAs vs. WAs not explained by known factors for 25 types of cancer. Studies reported that AAs have significantly increased risk for 13 types of cancer after consideration of SES, cancer stage at time of diagnosis, and treatment (continued)

Cancer	SES	Cancer stage at diagnosis	Treatment	Relative Risk (95% CI), AAs vs. WAs	Ref.
Ovarian, 2003–2007		Y	Y	1.29 (1.12–1.49)	74
Pancreatic				0.93 (0.83–1.04)	75
Pancreatic—adenocarcinoma	Y	Y	Y	1.00 (0.94–1.06)	76
Pancreatic				1.42 (1.28–1.58)	11
Prostate (meta-analysis)	Y	Y	Y	1.13 (1.00–1.27)	77
Prostate—55–84 y	Y			Approx 2	78
Prostate, advanced	Y	Y	Y	1.19 (1.05–1.35)	10
Prostate, meta-analysis	Y	Y	Y	1.15 (0.95–1.41)	79
Rectal		Y		1.27 (1.17–1.38)	58
Rectal		Y	Y	1.19 (1.09–1.29)	58
Rectal	Y	Y	Y	1.11 (1.02–1.20)	58
Renal				No difference	80
Testicular	Y	Y	Y	2.12	81
Thyroid (5-y survival, blacks vs. whites)				96.5% vs. 97.4%, p = 0.006	82
Vaginal		Y	Y	1.2 (1.1–1.4)	83

NSC, non-small cell; SES, socioeconomic status.

conditions for the elderly,[89-91] including diabetes and cardiovascular disease, influenza and pneumonia, and falls and fractures.

Secondary hyperparathyroidism due to osteoblastic metastases and hungry bone syndrome has been described with advanced prostate and breast cancer, it is likely that a vitamin D replete state may minimize such occurrences.[92] Bisphosphonates are commonly used in oncology. Pamidronate administration improved the secondary hyperparathyroidism due to "bone hunger syndrome" in a patient with osteoblastic metastases from prostate cancer. Coleman and McCloskey[93] suggest that bisphosphonates may prevent metastases and reduce the risk of disease recurrence. Based on animal data,[94] a vitamin D replete state may be helpful in reducing bisphosphonate induced osteonecrosis of the jaw.

Factors other than SES, stage at diagnosis, treatment, and vitamin D status might also explain the cancer survival disparities. For example, the lack of survival disparities for lung cancer may be due to a stronger effect from smoking than from vitamin D. Smoking cessation improves lung cancer survival rates associated with early-stage lung cancer.[95]

Obesity is significantly correlated with cancer risk for nearly all types of cancer listed in **Tables 1 and 2**.[96,97] AAs tend to have higher body mass index than WAs. One reason is that obesity is linked to poverty in the United States because of energy-dense but nutrient-poor foods are cheaper due to subsidies.[98] A second reason is that AAs have about twice the prevalence of apolipoprotein E ε4 (ApoE4) than WAs.[99] ApoE4 increases production of cholesterol in the liver and of insulin in the pancreas to store excess food as fat for those with sporadic food supplies, such as hunter-gatherers. Interestingly, overweight and obesity rates for white and black men differ little, whereas AA women are much heavier than WA women (http://www.cdc.gov/NCHS/data/hestat/obesity_adult_07_08/obesity_adult_07_08.pdf). Thus, obesity does not seem to be a likely explanation for cancer disparities among men but could be for women. On the other hand, serum 25(OH)D concentrations are inversely correlated with body mass index, which has implications for cancer risk.[100] Interestingly, for pancreatic cancer incidence, higher body mass index was significantly associated with risk for AA and WA men and WA women but with only insignificantly reduced risk for AA women.[11]

Cancer survival studies with respect to serum 25(OH)D concentrations at time of diagnosis offer strong evidence for a beneficial effect of vitamin D. All cancers with a beneficial effect of vitamin D on survival have been found inversely correlated with solar UVB doses, with the possible exception of chronic lymphocytic leukemia.[41] There are also studies from Norway indicating improved survival for those diagnosed with breast, colon, prostate cancer and Hodgkin lymphoma in summer compared with winter.[35]

The UVB-vitamin D-cancer hypothesis receives its strongest support from ecological studies.[19-24,27,28] Observational studies also provide good support if the various studies are examined carefully and a good reason is found for why many observational studies have not found a beneficial effect of vitamin D in reducing the risk of cancer. Nested case-control studies have a reduced strength since only a single serum 25(OH)D concentration measurement or oral intake assessment is made at time of enrollment, with follow-up periods lasting between 3 and 28 y.[101] As the follow-up time increases beyond about 3–7 y, the single measurement is less meaningful.[101,102] Case-control studies, on the other hand, use serum 25(OH)D concentration or vitamin D oral intake values at the time of diagnosis. A review of observational studies of breast and colorectal cancer incidence with respect to serum 25(OH)D concentration found statistically significant inverse correlations for breast cancer out to 3 y and for colorectal cancer out to 12 y of

follow-up.[101] Thus, the recently reported results from the Vitamin D Pooling Project study of rarer cancer types (endometrial, esophageal, gastric, ovarian, pancreatic, and renal cancer and non-Hodgkin lymphoma)[103] probably failed to find an inverse correlation between incidence of these cancers and prediagnostic serum 25(OH)D concentrations because the mean follow-up period was 6.63 y and because there were so few cases that the 95% confidence intervals were about 50%. The correlation between serum 25(OH)D concentrations measured at different times decreases with time, dropping to a regression coefficient of 0.40 after 14 y.[104]

Several ways exist to test the UVB-vitamin D-cancer hypothesis as an additional contributing factor for cancer survival disparities. One would be to measure serum 25(OH)D concentrations of newly diagnosed cancer patients and at several intervals during the course of the cancer. Another would be to supplement newly diagnosed cancer patients with sufficient vitamin D to bring serum 25(OH)D concentrations up to 40–80 ng/ml and compare results for those not supplemented, perhaps from previous patients in the same practice. A recent publication described the rationale for vitamin D supplementation,[105] which is being done in some cancer treatment centers.[106,107] Increasing serum 25(OH)D concentrations would also reduce the risk of severe sepsis associated with cancer surgery[108] as well as many other comorbid diseases.[89-91]

Study caveats. We acknowledge that while it appears very likely that vitamin D is an important and often ignored factor in the biology of cancer, the issue of cancer etiology is complex and is clearly multifactorial. Moreover, outcomes studies may have skewed results since AA men are less likely to participate in cancer screening trials.[109] Black women may be less physically active.[110] An inverse relationship between physical activity and breast cancer in AA women has been reported.[111] Some of the adverse cancer outcomes may relate to less than optimal care. Esnaola et al.[112] reported that AA patients are less likely to receive resection in non-metastatic rectal cancer. Rolnick et al.[113] demonstrated that AA colorectal cancer survivors are less likely to receive post-treatment colorectal surveillance. Similar findings have been found in prostate cancer.[114] These may not necessarily reflect racism in that physicians may make recommendations based on a patient's access to health care, presence of insurance, etc.[115] In addition, poor health literacy in AA women may also impact access to available health care strategies.[116]

Cultural differences may also play a role with cultural insensitivity among providers compounding the issue. Margolis et al.[117] demonstrated significant racial differences in belief prior to lung cancer surgery. Some of these differences result in refusal of surgery on the part of AA patients. AAs have less trust in their health providers and may not accept physicians' assertions regarding treatment.[117] Spiritually based health interventions may be more effective in AAs.[118] Van Ness et al.[119] indicates that lack of religiousness maybe associated with poor cancer survival in AA women. Church attendance may be associated with greater emotional and social support, which is linked to better outcomes in breast cancer.

We must also consider the possibility that apart from direct cellular benefits of vitamin D on cancer that vitamin D deficiency has indirect effects which are hard to quantify but may have a significant impact on cancer outcomes. Vitamin D deficiency is also associated with a higher prevalence of depression and neurocognitive symptoms, which makes patients intrinsically less likely to seek medical attention. Treating vitamin D deficiency may ameliorate symptoms of depression.[120]

Some risk factors such as diet can be modified and increased consumption of vegetables may decrease the risk of breast cancer in AAs, possibly by altering estrogen/progesterone receptor status.[121] Fortunately, it does appear that tumors are not intrinsically more aggressive in AAs.[122] In Veterans with equal access to health care, lung and colon cancer are not necessarily more aggressive diseases in AAs.[123] Dignam reported that black women, diagnosed at comparable disease stage as white women and treated appropriately, tend to experience similar breast cancer prognoses and survival.[124]

Some of the residual disparity for prostate cancer may be due to the higher prevalence of the ApoE4 allele among AAs than WAs,[99] which is related to increased cholesterol production. Cholesterol is an important risk factor for high-grade prostate cancer.[125] Increased low-density lipoprotein concentrations increased the risk of prostate cancer for AAs but not WAs.[126]

Conclusion

Lower serum 25(OH)D concentrations among AAs than WAs may explain many of the cancer survival disparities after consideration of SES, stage at time of diagnosis, and treatment. More research is required to confirm this hypothesis. If substantially correct, programs to increase serum 25(OH)D concentrations among AAs could reduce the cancer disparities. This approach would work not only for those of the ages where cancer is more likely but also for those younger. Vitamin D can reduce the risk of cancer at the initiation stage and in the advanced stages, as well as raising serum 25(OH)D concentrations to over 40 ng/ml shortly after cancer diagnosis. Given the biologic plausibility, the currently available evidence of beneficence, and the lack of harm with moderate Vitamin D replacement, we recommend Oncologists consider a more proactive stance on this issue pending additional studies.

Materials and Methods

Being a review, this analysis summarizes papers in the journal literature. Papers cited in this study came from the National Library of Medicine's PubMed database (http://www.pubmed.gov). As of December 28, 2011, a search for cancer disparity papers (search terms "cancer disparities survival, African-American") identified 457 articles. We reviewed the titles and abstracts of many of these. We examined in more detail those reporting hazard ratios for AAs vs. WAs for survival. The tables in this review do not include the component papers of meta-analyses cited. Thus, the papers listed in the tables are representative rather than exhaustive. We inspected the results in the papers, preferring those with disparities in survival that included all three factors—SES, stage at diagnosis, and treatment,

in addition to race—over those including fewer or none of these factors. We examined the papers to see whether survival was cancer-specific or all-cause.

In addition, papers reporting cancer survival with respect to serum 25(OH)D concentration were also sought.

Disclosure of Potential Conflicts of Interest

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