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THE RELATIONSHIP BETWEEN ULTRAVIOLET LIGHT EXPOSURE AND MORTALITY IN DIALYSIS PATIENTS

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Abstract

Background—Emerging data suggest that reduced exposure to ultraviolet (UV) radiation is associated with increased mortality in the general population. To date, there has not been examination of the association between UV exposure and mortality in dialysis patients.

Methods—We examined the association between UV index, a proxy of UV exposure, and all-cause mortality among 47,286 US dialysis patients (entry period 2001–2006, with follow-up through 2009) from a large national dialysis organization using multivariable Cox regression. The UV index was ascertained by linkage of individual patients' residential zip codes to National Oceanic and Atmospheric Administration data, and was categorized as low (0–<3), moderate (3–<5), moderate-high (5–<6), high (6–<7), and very-high (≥7). In secondary analyses, we examined the UV index—mortality association within subgroups of age (<65 vs. ≥ 65 years old), sex, and race (white vs. non-white).

Results—The study population's mean±SD age was 60±16 years old and included 46% women and 56% diabetics. Compared to patients residing in moderate-high UV index regions, those residing in high and very-high UV index regions had lower mortality risk: adjusted HRs 0.84 (95% CI) 0.81–0.88 and 0.83 (95% CI) 0.75–0.91, respectively. A similar inverse association between UV index and mortality was observed across all subgroups, although there was more pronounced reduction in mortality among whites vs. non-whites.

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Conflicts of Interest:

KKZ was medical director of the DaVita Harbor-UCLA Long Beach from 2007–2012. BBS, ES, JLTC, CPK, and CMR have nothing to declare.

Conclusion—These data suggest that dialysis patients residing in higher UV index regions have lower all-cause mortality compared to those living in moderate-high UV regions. Further studies are needed to determine mechanisms underlying the UV index—mortality association.

Keywords

Dialysis; environment; mortality; ultraviolet radiation; vitamin D

INTRODUCTION

There has been increasing interest in the impact of environmental exposures such as ultraviolet (UV) radiation exposure on human health. UV radiation has been classified as a human carcinogen by the U.S. Department of Health and Human Services and the World Health Organization given its causal associations with skin cancer.[1] However, emerging data from the general population suggest that increased UV exposure is associated with decreased risk of certain non-dermatologic malignancies (e.g., prostate, breast, non-Hodgkin's lymphoma) as well as reduced cardiovascular and all-cause mortality.[2–4] It has been hypothesized that increased endogenous synthesis of vitamin D stimulated by UV exposure may be a mechanistic link for this paradoxical association. Indeed, UV irradiance is an important determinant of vitamin D biosynthesis and status in the general population.[5, 6]

Vitamin D deficiency is highly prevalent in chronic kidney disease (CKD) patients including those who are dialysis-dependent,[7–9] and it is associated with increased risk of adverse cardiovascular surrogates (e.g., coronary artery calcification,[10] atherosclerosis, [11] endothelial dysfunction[11]), cardiovascular events,[12] and mortality.[13, 14] Emerging data suggest that, despite impaired conversion of inactivated to activated vitamin D in dialysis patients, both solar UV exposure[15–18] and artificial UV exposure[19] may be important predictors of vitamin D status in this population. Notwithstanding the known impact of vitamin D on hard outcomes in dialysis patients, there has not been examination of the association between UV exposure and mortality risk in this context.

We hypothesized that dialysis patients residing in areas of high UV exposure have decreased mortality risk compared to those living in areas of low UV exposure. To better inform the field, we sought to examine the association between UV exposure and all-cause mortality within a large, contemporary cohort of US dialysis patients with comprehensive capture of sociodemographic, comorbidity, and laboratory data.

MATERIALS AND METHODS

Study Population

We examined administrative data from all end-stage renal disease patients who underwent hemodialysis or peritoneal dialysis in one of the DaVita Healthcare Partners Inc. outpatient dialysis facilities during an entry period of July 1, 2001 to June 30, 2006, with follow-up through June 30, 2009. The creation of this cohort has been previously described.[20] The study was approved by the Institutional Review Committees of the Los Angeles Biomedical

Research Institute at Harbor-UCLA and DaVita Clinical Research. The requirement for a written consent form was waived because of the large sample size, anonymity of the patients studied, and the non-intrusive nature of the research.

The first (baseline) study quarter was the calendar quarter in which each patient's dialysis vintage was >45 days during at least half of that quarter. Patients were included provided that they were ≥18 years old during the baseline quarter, and had available residential zip code and UV exposure data.

Ultraviolet Exposure Ascertainment

We sought to examine the association between forecasted ambient UV radiation, quantified by the UV index, and mortality. The UV index was first proposed by Environment Canada and subsequently adopted and standardized by the World Health Organization and the World Meteorological Organization in 1994. It is used to predict the UV radiation intensity reaching the earth's surface, and has been used as a proxy of UV exposure in prior epidemiologic studies.[21–23] The calculation of UV index takes into account stratospheric ozone concentration, cloud coverage, altitude, sun's position, surface albedo, tropospheric aerosol loading[24], and it is additionally adjusted for the variations in skin sensitivity to different wavelengths of light, based on the McKinlay-Diffey erythema action spectrum.[25] The resulting value is scaled by a numerical factor and rounded to the nearest whole number, ranging from zero to the mid-teens. A higher UV index corresponds to more intense UV radiation incident at the surface of a particular location.[26]

The National Oceanic and Atmospheric Administration (NOAA) National Weather Center provides daily UV index forecasts for 58 major US cities. Each US state is represented by at least one of these 58 cities, with additional representation in California, Florida, New York, Pennsylvania, and Texas. UV data for each city was applied to all zip codes within the cities' county boundaries, for an aggregate of 5,425 zip codes. UV index values were linked to each individual DaVita dialysis patient using their residential zip codes, ascertained at baseline and updated quarterly. While UV index may be forecasted for any time of the day or year, in this study, each patient's UV index represents the average of the annual noon-time UV index values estimated over his/her respective follow-up period. In primary analyses, UV indices were stratified into five groups, adapted from the Environmental Protection Agency's UV index categories: low (0–<3), moderate (3–<5), moderate-high (5–<6), high (6–<7), and very-high (≥7).

Outcome Ascertainment

The primary outcome of interest was all-cause mortality which was ascertained from the DaVita database and through United States Renal Data System database linkage. Patients were followed for the outcome of interest until death, or censoring for kidney transplantation or end of the study period (June 30, 2009).

Dialysis Treatment and Laboratory Covariates

Dialysis vintage was defined as the duration of time between the first day of dialysis treatment and the first day that the patient entered the cohort. To minimize measurement

variability and to address the effect of short-term variation in dietary and fluid intake on weight and laboratory measurements, we averaged all repeated measures for each patient during any given calendar quarter (i.e., over 13 consecutive weeks or 3 months). Blood samples were drawn using uniform techniques in all dialysis clinics and were transported to the DaVita Laboratory in Deland, Florida typically within 24 hours, and were measured by automated and standardized methods. Most laboratory values were measured monthly, and serum ferritin and intact parathyroid hormone (PTH) levels were measured at least quarterly. Hemoglobin was measured weekly to bi-weekly in most patients. Most blood samples were collected pre-dialysis with the exception of the post-dialysis serum urea nitrogen.

Statistical Methods

Baseline characteristics between UV index categories were compared using non-parametric tests for linear trend. The associations between UV index and mortality were evaluated using Cox proportional hazards regression models. For each analysis, three models were examined with incremental multivariable adjustment for baseline covariates:

- **a.** Model 1 which included the entry calendar quarter;
- **b.** Model 2 which included covariates from Model 1, as well as age, sex, dialysis modality, race/ethnicity (African–Americans, non-Hispanic Caucasians, Hispanics, Asians, and other), diabetes mellitus, dialysis vintage, primary insurance, marital status, and dialysis dose (i.e., single pool kt/v);
- **c.** Model 3 which included covariates from Model 2, as well as body mass index, baseline comorbidities (alcohol dependence, active smoking, cardiac failure, chronic-obstructive pulmonary disorder, cerebrovascular disease, and peripheral vascular disease), and the following laboratory covariates: serum albumin, calcium, bicarbonate, creatinine, ferritin, hemoglobin, lymphocyte percentage, normalized protein catabolic rate, phosphorus, white blood cell count, alkaline phosphatase, and PTH.

UV index-mortality associations were examined within subgroups of age (<65 years vs. ≥65 years), sex, and race (white vs. non-white). We employed a complete case analysis approach in which analyses were restricted to patients with available data for all covariates used in each respective model, although missing data was <1% for most laboratory and demographic variables. All p-values were 2-tailed ($p<0.05$). Analyses were conducted using Stata version 10.1 (Stata Corporation, College Station, Texas).

RESULTS

Baseline Characteristics

After excluding patients who were <18 years old or who had missing age data; those who did not maintain ≥45 days of thrice-weekly dialysis treatment during the baseline calendar quarter; and those with missing zip code-linked UV index data, the final source cohort consisted of 47,286 dialysis patients. Supplementary Figure 1 shows the distribution of dialysis patients according to their respective UV index categories, with the majority of patients residing in areas of moderate to high UV regions.

Baseline demographic, clinical and laboratory data of dialysis patients across the five UV index categories were examined (Table 1). Compared to patients residing in the lowest UV index category, those residing in the highest category were more likely to be African-American, Hispanic, divorced, treated with hemodialysis, and of shorter dialysis vintage; had a higher prevalence of diabetes, atherosclerotic heart disease, cardiac failure, and peripheral vascular disease; and had higher mean residual renal function, ferritin, and PTH levels.

Ultraviolet Index and Mortality in Dialysis Patients

The association between residential UV index divided into five categories and all-cause mortality was examined in three Cox regression models with incremental levels of multivariable adjustment (Figure 1 and Table 2). Compared to patients living in moderate-high UV index areas, those living in high to very-high UV index areas had decreased mortality risk, whereas patients residing in moderate and low UV index areas had decreased and similar mortality risk, respectively.

Subgroup Analyses

The UV index—mortality association was examined in patients stratified by age (<65 vs. ≥ 65 years old), sex, and race (white vs. non-white). A similar inverse association between UV index and mortality was observed in all subgroups, although there appeared to be a more pronounced reduction in mortality among whites compared to non-whites (Figure 2 and Supplementary Table 1).

DISCUSSION

To our knowledge, this is the first study to examine the association between UV exposure and mortality in a contemporary cohort of US dialysis patients. In the general population, there is evidence that solar UV radiation is causally associated with skin cancer (e.g., malignant melanoma, basal and squamous cell cancer) via direct induction of DNA damage and indirect effects on immune suppression,[27, 28] and it has been deemed to be a carcinogen by the International Agency for Research on Cancer.[29] However, emerging data suggest that UV radiation may also have potential health benefits. A number of ecologic and cohort studies have suggested that there is an inverse association between UV radiation (defined as UV index, solar UV-B radiation, and erythemogenic UV radiation in these studies) with cancer incidence and mortality (renal,[4, 30] prostate,[3, 4, 31] breast,[4, 31, 32] colon,[4, 30–32], and rectal[4, 30]). Furthermore, in a recent prospective cohort study of 38,472 Swedish women, participants who reported higher levels of prior natural and artificial UV exposure (i.e., prior history of sunburn, sunbathing, and solarium use) had decreased all-cause and cardiovascular mortality.[2] In our study, UV index was employed as an objective metric of forecasted solar radiation, and we observed that individuals living in higher UV exposure regions had decreased mortality risk compared to those living in low to moderate UV exposure regions.

Increased biosynthesis of vitamin D has been suggested as a potential mechanistic link between higher UV indices and decreased cancer incidence and cardiovascular mortality. In

terms of the former outcome, vitamin D has been associated with decreased cancer risk vis-a-vis improved cell differentiation and apoptosis, anti-angiogenesis, decreased metastases, and decreased risk of viral infection-associated malignancies in some[33–35], but not all studies[36]. In terms of the latter outcome, multiple observational studies have reported an inverse association between vitamin D levels and greater risk of adverse cardiovascular surrogates, cardiovascular events and mortality in populations with[12–14] and without[37–39] chronic kidney disease (CKD). Solar UV-B radiation promotes the conversion of 7-dehydrocholesterol to pre-vitamin D_3 in skin tissue, which then isomerizes to vitamin D_3 (i.e., cholecalciferol). Vitamin D_3 is then transported to the liver where it undergoes hydroxylation by cytochrome p450 enzymes to become 25-hydroxy-vitamin D (i.e., calcidiol), the major circulating form of vitamin D. Inactive 25-hydroxy-vitamin D is then converted into active 1,25-dihydroxy-vitamin D (i.e., calcitriol), by the 1-α hydroxylase enzyme present in various parts of the nephron.[40] Although 1,25-dihydroxy-vitamin D production is downregulated in advanced CKD as a result of hyperphosphatemia,[41] uremia,[42, 43] metabolic acidosis,[44] and elevated fibroblast growth factor-23,[45, 46] experimental and clinical studies have shown that administration of 25-hydroxy-vitamin D, even in anephric individuals,[18] is associated with significant increases in activated vitamin D. This may be due to the presence of 1-α hydroxylase in other tissues (e.g., skin, lymph nodes, gastrointestinal tract, pancreas, heart, and adrenal glands) as an extra-renal source of activated vitamin D.[47, 48]

Cardiovascular disease is the leading cause of death in CKD, and vitamin D deficiency is associated with an increased risk of cardiovascular risk factors (e.g., albuminuria[49]), adverse cardiovascular surrogates (e.g., coronary artery calcification,[10] atherosclerosis,[11] endothelial dysfunction[11]) as well as increased risk of cardiovascular events[12] and all-cause mortality in this population.[13, 14] Observational studies have suggested that treatment with activated vitamin D reduces all-cause and cardiovascular mortality in patients with CKD, including those who are non-dialysis dependent and those receiving dialysis.[50–54] Although several studies suggest 25-hydroxy-vitamin D treatment may have benefits on cardiovascular surrogates in CKD patients,[55, 56] there have not been any well-designed randomized controlled trials or large observational cohort studies examining hard outcomes in this context.

Emerging data suggest that reduced sunlight exposure may be a predictor of vitamin D deficiency in dialysis patients,[17] and that artificial UV radiation may be an alternative source for vitamin D repletion in this context. In an observational cohort study of 15 dialysis patients, narrow-band UV-B treatment over a 3-week period resulted in a significant increase in serum 25-hydroxy and 1,25-dihydroxy-vitamin D levels.[19] Although dialysis patients may be less likely to participate in outdoor physical activity and hence have reduced natural UV exposure,[57, 58] even brief durations of solar or artificial UV exposure have been shown to significantly increase vitamin D levels in the general population[59–62]; further study is needed to determine if natural UV radiation may be a viable source of vitamin D repletion in dialysis patients. Due to data limitations, we were not able to directly ascertain patients' frequency or duration of outdoor activity, other factors that modify UV exposure (e.g., photosensitizing medications or photo-protective clothing), or vitamin D levels in our study; however, it is plausible that patients residing in higher UV index regions

experience greater solar UV radiation exposure and subsequent synthesis of vitamin D. Future studies directly measuring solar UV radiation exposure, serum vitamin D levels, and cardiovascular outcomes in CKD patients are needed.

When we examined associations between UV index and mortality across subgroups of race, higher UV index categories were associated with a more potent survival benefit among white patients compared to non-whites in the highest UV index category (≥7). While genetic polymorphisms may partially account for variations in total vitamin D level across racial groups [63], light-skinned individuals experience greater UV-B absorption and subsequent vitamin D synthesis as a result of their reduced melanin skin content, compared to those who are non-white.[64, 65]

Strengths of our study include the examination of a large, contemporary US dialysis population with extended follow-up; comprehensive availability of clinical data allowing for adjustment of multiple confounders; examination of individual patients' residential UV indices; and use of a validated assessment of UV exposure that accounts for potential confounders such as altitude. However, several limitations of our study bear mention. First, our analyses examined quarterly residential UV index only, and did not account for patients who may have migrated over time within that period. Second, we are unable to confirm that an individual's residential UV index, which is a forecast, directly correlates with the patient's actual UV exposure. Third, given that the National Oceanic and Atmospheric Administration measures UV index in major US cities only, our study cohort may not be representative of dialysis patients living in outlier or rural regions. Fourth, while we attempted to adjust for broad markers of nutritional status (e.g., normalized protein catabolic rate, serum albumin) in our multivariable models, due to data limitations we were unable to account for more granular nutritional variables (e.g., diet, nutritional supplements) that may confound the UV index—mortality association. For example, there may be regional variation in dietary intake (including foods that are supplemented with vitamin D), or utilization of vitamin D supplements that are also associated with mortality.[66] Lastly, as with all observational studies, we cannot confirm that there is a causal association between UV index and mortality.

Our data suggest that higher UV index is associated with survival benefit, and that these associations may be even more pronounced among dialysis patients vs. the US general population. Further studies are needed to confirm findings, and to determine the mechanistic pathways by which UV index is associated with mortality risk in dialysis patients.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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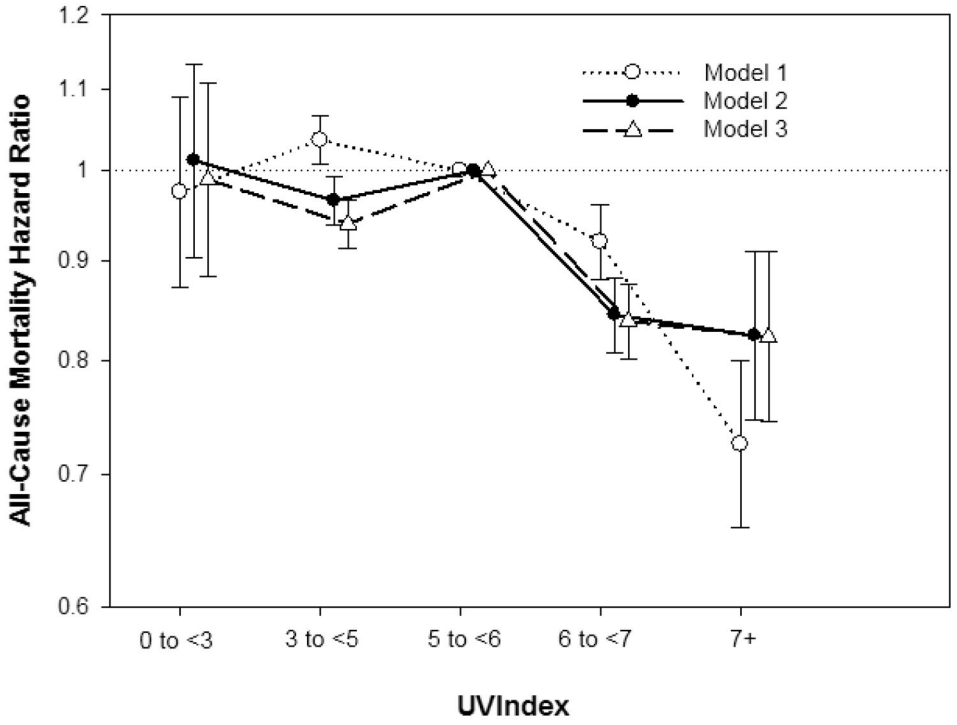
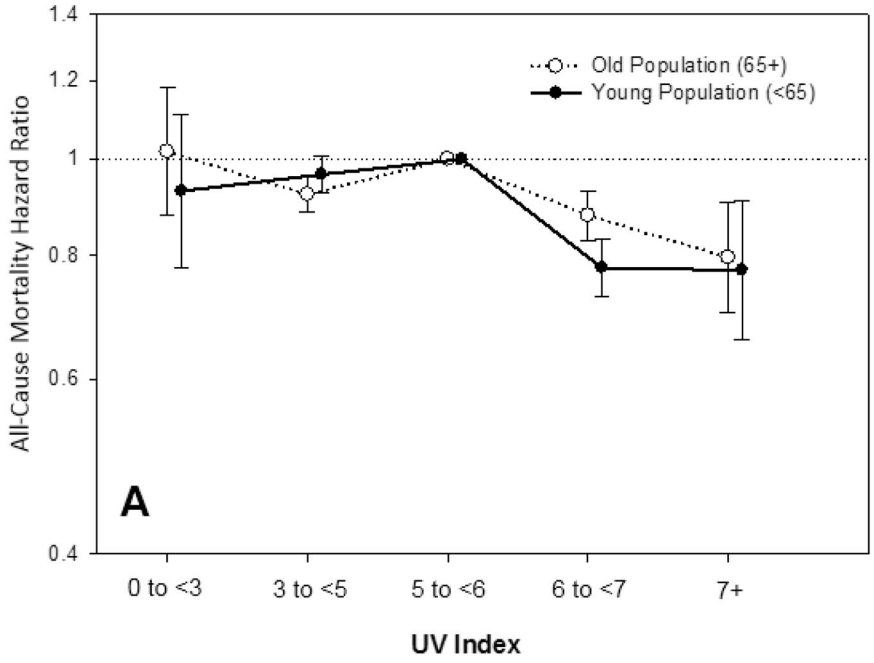
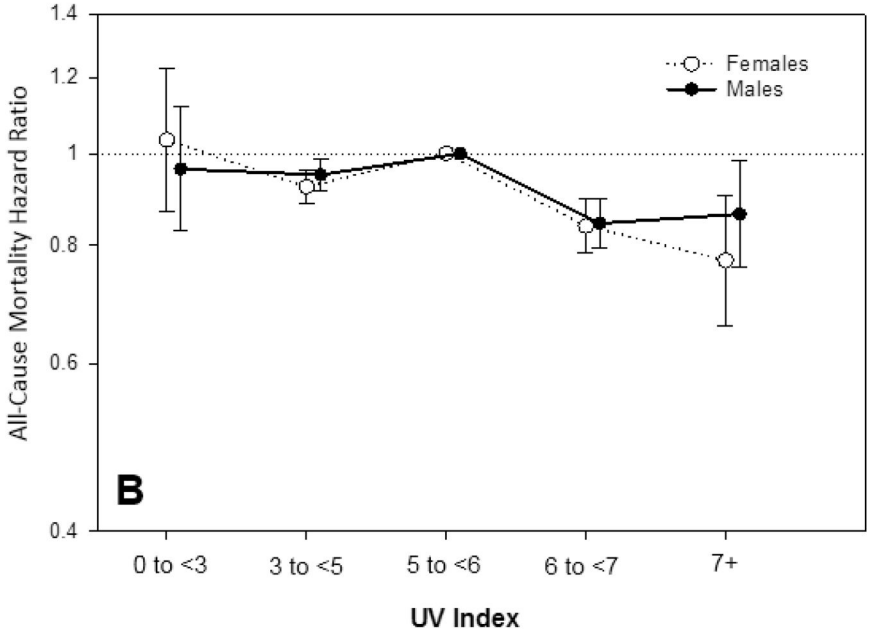


Figure 1. Association between residential ultraviolet (UV) index divided into five categories (low: <3; moderate: 3–<5; moderate-high: 5–<6; high: 6–<7; and very-high: ≥7) with all-cause mortality in dialysis patients (reference group: UV index 5–<6)

Model 1 included UV index category and entry calendar quarter. Model 2 included covariates from Model 1, as well as age, sex, dialysis modality, race/ethnicity, diabetes mellitus, dialysis vintage, primary insurance, marital status, and dialysis dose (i.e., single pool kt/v). Model 3 included covariates from the Model 2, baseline comorbidities (alcohol dependence, active smoking, cardiac failure, chronic-obstructive pulmonary disorder, cerebrovascular disease, and peripheral vascular disease), body mass index, serum albumin, calcium, bicarbonate, creatinine, ferritin, hemoglobin, lymphocyte percentage, normalized protein catabolic rate, phosphorus, white blood cell count, alkaline phosphatase, and parathyroid hormone.





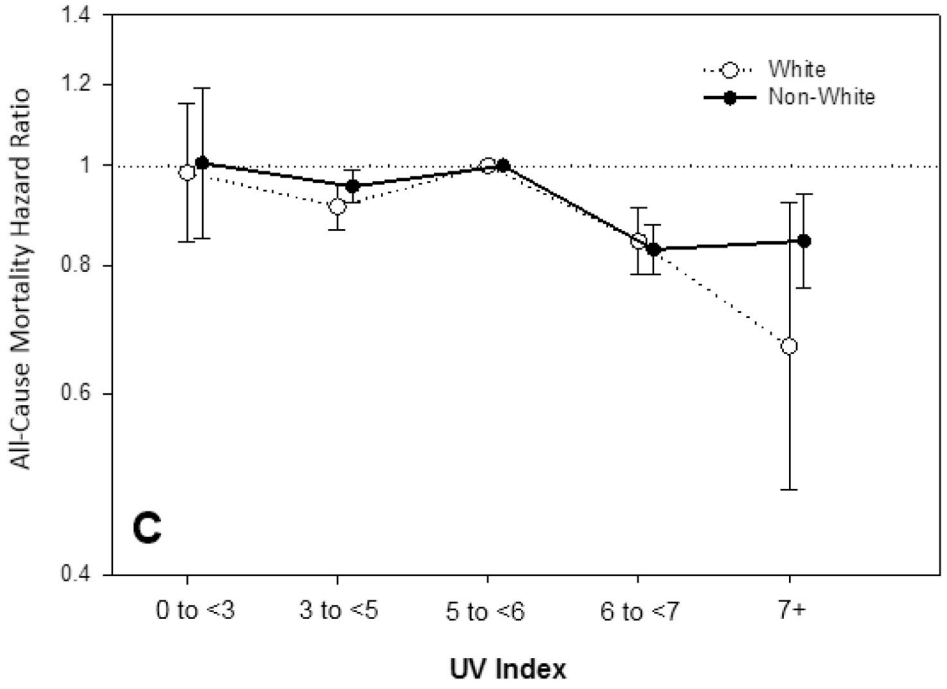


Figure 2. Association between residential ultraviolet (UV) index divided into five categories (low: <3; moderate: 3–<5; moderate-high: 5–<6; high: 6–<7; and very-high: ≥7) with all-cause mortality in dialysis patients within subgroups of age (<65 years vs. ≥65 years), sex (female vs. male), and race (white vs. non-white)

Models included UV index category, entry calendar quarter, age, sex, dialysis modality, race/ethnicity, diabetes mellitus, dialysis vintage, primary insurance, marital status, dialysis dose (i.e., single pool kt/v), baseline comorbidities (alcohol dependence, active smoking, cardiac failure, chronic-obstructive pulmonary disorder, cerebrovascular disease, and peripheral vascular disease), body mass index, serum albumin, calcium, bicarbonate, creatinine, ferritin, hemoglobin, lymphocyte percentage, normalized protein catabolic rate, phosphorus, white blood cell count, alkaline phosphatase, and parathyroid hormone.

Table 1

Baseline characteristics among dialysis patients stratified by residential ultraviolet (UV) index category.

		UV Index					
	Total n= 47,286	**<3 (n=595)**	**3–<5 (n= 19,941)**	**5–<6 (n= 18,630)**	**6–<7 (n= 7,206)**	**7+ (n= 914)**	**p-value**
Age, mean (SD)	60 (16)	60 (16)	60 (16)	59 (16)	60 (16)	61 (16)	0.2
Female (%)	46	40	45	50	44	41	0.9
Diabetes mellitus (%)	56	49	54	49	58	55	<0.001
Dialysis Modality (%)							
Hemodialysis	95	93	96	94	94	99	0.01
Peritoneal Dialysis	5	7	4	6	6	1	
Race and Ethnicity (%)							
White	27	50	31	22	30	13	<0.001
Black	41	22	50	35	30	39	<0.001
Hispanic	21	4	9	28	31	45	<0.001
Asian	4	10	2	7	4	~0	<0.001
Other	6	12	6	7	5	3	<0.001
Vintage (%)							
<6 months	12	6	12	8	21	15	<0.001
6–<24 months	29	25	29	22	46	32	<0.001
2–<5 years	35	41	35	40	22	30	<0.001
≥5 years	24	28	24	29	11	23	<0.001
Primary Insurance (%)							
Medicare	58	49	61	55	60	52	<0.001
Medicaid	8	3	7	10	8	5	<0.001
Private Insurance	10	24	8	13	4	11	<0.001
Other	14	16	15	10	23	28	<0.001
Marital Status (%)							
Married	36	44	34	35	44	41	<0.001
Divorced	6	4	7	6	7	10	0.007
Single	28	26	30	25	29	26	<0.001
Widowed	11	10	12	11	12	10	0.09

		UV Index					
	Total n= 47,286	**<3 (n=595)**	**3–<5 (n= 19,941)**	**5–<6 (n= 18,630)**	**6–<7 (n= 7,206)**	**7+ (n= 914)**	**p-value**
spKt/V, mean (SD)	1.50 (0.35)	1.61 (0.32)	1.48 (0.33)	1.49 (0.35)	1.53 (0.39)	1.59 (0.36)	<0.001
Residual Renal Function (ml/min), mean (SD)	2.77 (2.5)	1.99 (1.7)	2.64 (2.50)	2.60 (2.25)	3.26 (2.90)	3.30 (2.39)	<0.001
Comorbidities (%)							
Active Smoking	4	4	5	3	3	2	<0.001
AHD	16	19	18	13	16	24	<0.001
Alcohol Dependence	1	1	1	1	1	1	<0.001
Cardiac Failure	23	20	24	22	24	30	0.09
COPD	4	5	4	3	4	4	<0.001
CVD	6	7	7	5	6	7	0.004
Drug Use	1	1	2	1	1	1	<0.001
Non-ambulatory State	3	1	3	3	3	4	<0.001
Malignancy	3	3	4	2	3	5	<0.001
PVD	8	10	9	6	9	16	0.002
Serum or Blood Levels, mean (SD)							
Ferritin (ng/mL)	526 (504)	519 (411)	497 (479)	566 (533)	481 (483)	582 (521)	<0.001
Hemoglobin (g/dL)	11.9 (1.4)	12.0 (1.2)	11.9 (1.4)	11.9 (1.3)	12.1(1.4)	12.2 (1.2)	<0.001
TIBC (mg/dL)	208 (46)	211 (46)	208 (47)	206 (46)	214 (46)	204 (41)	<0.001
Albumin (g/dL)	3.67 (0.47)	3.71 (0.44)	3.67 (0.48)	3.69 (0.46)	3.65 (0.48)	3.72 (0.45)	0.3
Calcium (mg/dL)	9.2 (0.7)	9.3 (0.8)	9.2 (0.7)	9.2 (0.7)	9.2 (0.7)	9.3 (0.7)	0.5
Intact PTH (pg/ml)	375 (391)	340 (347)	384 (405)	369 (380)	366 (377)	447 (493)	0.006
Phosphorus (mg/dL)	5.6 (1.5)	5.8 (1.5)	5.6 (1.5)	5.6 (1.5)	5.5 (1.5)	5.6 (1.4)	0.5
Creatinine (mg/dL)	8.5 (3.5)	8.9 (3.3)	8.6 (3.5)	8.7 (3.6)	7.6 (3.3)	8.8 (3.5)	<0.001
nPCR (g/kg/day)	0.96 (0.26)	0.97 (0.26)	0.94 (0.25)	0.97 (0.26)	0.94 (0.26)	1.00 (0.27)	0.002
BMI (kg/m2)	26.6 (6.9)	26.7 (8.0)	26.8 (7.0)	26.4 (6.9)	26.6 (6.5)	26.6 (6.3)	0.1
WBC ($\times 10^3$/ul)	7.3 (2.4)	7.7 (2.8)	7.3 (2.5)	7.4 (2.4)	7.5 (2.3)	7.4 (2.3)	<0.001
Lymphocyte %	21 (8)	20 (8)	21 (8)	21 (8)	21 (8)	23 (8)	<0.001
Bicarbonate (mg/dL)	22.4 (3.1)	23.2 (3.4)	22.2 (3.1)	22.5 (3.0)	22.9 (3.2)	22.1 (3.1)	<0.001

* p-values were calculated using non-parametric tests of linear trend.

Abbreviations: SD: standard deviation; AHD: atherosclerotic disease; COPD: chronic-obstructive pulmonary disease; CVD: cerebrovascular disease; PVD: peripheral vascular disease; TIBC: total iron binding capacity; PTH: parathyroid hormone; nPCR: normalized protein catabolic rate; BMI: body mass index; WBC: white blood cell count

Table 2

All-cause mortality hazard ratios (95% confidence intervals) in dialysis patients across ultraviolet (UV) index categories.

UV index	n=47,286	Model 1* HR (95% CI)	Model 2† HR (95% CI)	Model 3†† HR (95% CI)
<3	595	0.98 (0.87, 1.09)	1.01 (0.90, 1.13)	0.99 (0.88, 1.11)
3–<5	19,941	1.04 (1.01, 1.07)	0.97 (0.94, 0.99)	0.94 (0.91, 0.97)
5–<6	18,630	1.00	1.00	1.00
6–<7	7,206	0.92 (0.88, 0.96)	0.84 (0.81, 0.88)	0.84 (0.80, 0.88)
7+	914	0.73 (0.66, 0.80)	0.82 (0.75, 0.91)	0.82 (0.74, 0.91)

*Model 1 included UV index category and entry calendar quarter.

†Model 2 included covariates from Model 1, as well as age, sex, dialysis modality, race/ethnicity, diabetes mellitus, dialysis vintage, primary insurance, marital status, and dialysis dose (i.e., single pool kt/v).

††Model 3 included covariates from Model 2, baseline comorbidities (alcohol dependence, active smoking, cardiac failure, chronic-obstructive pulmonary disorder, cerebrovascular disease, and peripheral vascular disease), body mass index, serum albumin, calcium, bicarbonate, creatinine, ferritin, hemoglobin, lymphocyte percentage, normalized protein catabolic rate, phosphorus, white blood cell count, alkaline phosphatase, and parathyroid hormone.