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Association of Height with Elevated Mortality Risk in ESRD: Variation by Race and Gender

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ABSTRACT

The association of adult height with mortality has been extensively investigated in the general population, but little is known about this relationship among dialysis patients. We explored the relationship between height and mortality in a retrospective cohort study of 1,171,842 adults who began dialysis in the United States from 1995 to 2008 and were followed until December 31, 2010. We evaluated height-mortality associations in sex-specific quintiles of increasing height (Q1–Q5) using multivariable Cox regression models adjusted for demographics, comorbid conditions, lifestyle and disability indicators, socioeconomic status, and body weight. For men, compared with the referent quintile (Q1 <167 cm), successive height quintiles had significantly increased hazard ratios (HRs [95% confidence interval]) for mortality: 1.04 (1.02–1.06), 1.08 (1.06–1.10), 1.12 (1.11–1.14), and 1.18 (1.16–1.20) for Q2–Q5, respectively. For women (referent Q1 <155 cm), HRs for mortality were 1.00 (0.99–1.02), 1.05 (1.03–1.06), 1.05 (1.03–1.07), and 1.08 (1.06–1.10) for Q2–Q5, respectively. However, stratification by race showed the pattern of association differed significantly by race ($P < 0.001$ for interaction). For black men, unlike other race groups, height only associated with mortality in Q5, with an HR of 1.06 (1.02–1.09). For black women, HRs for mortality were 0.94 (0.91–0.97), 0.98 (0.95–1.02), 0.96 (0.93–0.99), and 0.99 (0.96–1.02) for Q2–Q5, respectively. These results indicate tallness is associated with higher mortality risks for adults starting dialysis, but this association did not extend to black patients.

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Adulthood height is an anthropometric measurement that is determined by one's genetic makeup in addition to the interplay of several childhood and adolescence environmental factors including intercurrent illness, nutrition, and socioeconomic circumstances.^{1–5} Therefore, it is not surprising that the attained adult height is considered an important marker of early life health. Prospective population-based epidemiology studies, in general, have found an inverse association between adult height and the risk of death from all causes,^{6–9} supporting the hypothesis that early life and childhood factors affect survival in adulthood. Although the evidence linking tallness to an increased life expectancy is generally robust, these findings have not been consistently demonstrated in all studies.^{9–11} Furthermore, cause-specific analyses have found that increasing height is associated

with lower mortality from coronary disease but higher mortality from specific cancers.^{10–15} These divergent associations of height with mortality would suggest that the relationships between height and death are quite complex and may influence survival through potentially different mechanisms.¹⁰

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Height measurements are routinely captured in patients who develop ESRD and require dialysis therapies.¹⁶ Surprisingly, however, few published studies have explored the nature of the relationship of adult height with mortality among patients undergoing dialysis.¹⁷ Most published studies to date have evaluated the association of several anthropometric measures of health including weight, body mass index and waist circumference with major outcomes in order to examine their clinical importance.^{18–22} However, to the best of our knowledge none of these have explored the individual contribution of height to mortality in a sufficiently robust manner. Defining the nature of height-mortality relationship in ESRD would help us better understand the biologic importance of height as an index of childhood health and as a prognostic indicator of patient survival. For example, it is unclear if the survival benefit of tallness over shortness observed in the general population is maintained following the initiation of dialysis. Second, it remains to be determined whether associations of height with mortality can be accounted for by burden of illness present at the start of dialysis or variation in care patterns and treatment strategies prior to or after the initiation of dialysis.^{23–27} Third, given the importance of race in survival analysis in ESRD, it is tempting to speculate that any height-mortality differences might vary across existing racial subgroups.

To improve our understanding of anthropometric measures and their relationships with survival, we explored associations of adulthood height with mortality in a large contemporary cohort of patients from the US Renal Data System (USRDS) who began dialysis from 1995 to 2008. We hypothesized that tallness was associated with better survival as observed in the general population and that any apparent height-mortality relationships were independent of pre-existing baseline health status, socioeconomic circumstances, and predialysis care patterns.

RESULTS

Baseline Characteristics of Study Cohort

The study cohort included 1,171,842 individuals who commenced dialysis therapy between 1995 and 2008 (Figure 1). The mean age of subjects was 62.9 years, 54% were male, and the majority was white. The average height (\pm SD) for men and women was 173.9 (9.6) cm and 160.6 (8.6) cm, respectively. Black men were the tallest at 175.2 (9.8) cm followed by white 173.8 (9.3) cm and American Indian/Alaska native 173.8 (8.7) cm, while Asian men were the shortest at 166.4 (9.0) cm. Similarly, black women were significantly taller than white women and American Indian/Alaska native (162.3 [8.6] cm versus 160.0 [8.4] cm and 160 [7.9] cm, respectively) while Asian women were significantly shorter at 155 (8.5) cm. The average age decreased with increasing height quintiles for both men and women and the age-adjusted characteristics of adult men and women by height quintile are presented in Tables 1

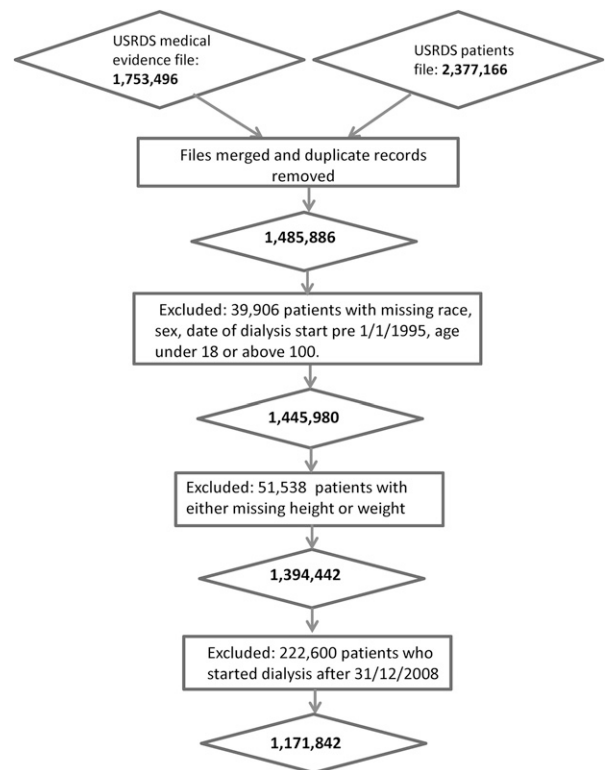


Figure 1. Selection process of the study population from merging of the USRDS standard analysis files.

and 2. Taller men and women were more likely to be black, non-Hispanic, have higher mean body weight, serum creatinine, and serum albumin than shorter individuals. Peripheral vascular disease, chronic lung disease, and malignancy were more common in tall men and women. Predialysis care including visits from a nephrologist or dietitian was more common in tall men and women as was full or part employment.

Age-Adjusted Mortality Rates Across Height Quintiles by Race and Sex

Patients were followed up for an average of 1.63 years. A total of 473,638 (40.42%) patients died, 65,799 (5.62%) were transplanted, and 5654 (0.48%) were lost to follow-up. Among men, mortality rates increased significantly with rising quintile of height although there was significant heterogeneity across race groups (Figure 2A). Among white, and to a lesser extent Asian and American Indians/Alaska natives, increases in death rates were observed with rising height quintile. However for black race, rates decreased significantly from the first to the fifth quintile. For women, the pattern of association was similar but not as striking (Figure 2B).

Associations of Height with Mortality by Sex and Race

The age-adjusted and multivariable-adjusted hazard ratios (HRs) for death with increasing quintile of height are shown for men in Table 3. With adjustment for age, the HRs increased significantly and were highest for the highest quintile (HR,

Table 1. Baseline characteristics of men by height quintiles in the United States dialysis population: 1995–2008^a

	N ^f	Q1 All men (n=636,594)	Q2 167–172 cm (n=117,543)	Q3 173–177 cm (n=140,559)	Q4 178–181 cm (n=129,553)	Q5 ≥182 cm (n=130,648)	P value for trend
Demographics							
Age (years) ^b	636,594	62.3 (15.4)	63.7 (16.0)	63 (15.1)	62 (15.0)	59.3 (15.0)	<0.001
Race (%)							
White	636,594	68.3	66.9	69.7	70.9	67.2	0.02
Black	636,594	27	22.2	26.8	26.8	31.4	<0.001
Asian	636,594	3.7	10.0	2.4	1.3	0.7	<0.001
American Indian/Alaska native	636,594	1.0	0.9	1.10	0.9	0.7	<0.001
Hispanic (%)	634,428	12.2	25.0	10.6	6.5	3.5	<0.001
Primary cause of ESRD (%)							
Diabetes	636,594	42.7	44.8	42.1	41.7	41.5	<0.001
Hypertension	636,594	29.1	29.7	29.9	29.0	28.1	<0.001
Glomerulonephritis	636,594	9.1	7.9	8.6	9.5	9.4	<0.001
Cystic kidney disease	636,594	2.0	1.3	1.7	2.2	2.9	<0.001
Other urologic disease	636,594	2.8	2.8	2.8	2.9	2.8	0.03
Other cause	636,594	10.2	8.9	10.4	10.7	11.2	<0.001
Unknown cause	636,594	4.1	4.5	4.1	4.0	4.0	<0.001
Comorbid conditions (%)							
Diabetes (as comorbid condition)	636,594	50.2	51.5	49.8	49.6	49.7	0.07
Hypertension	636,586	78.8	77.9	79.0	78.9	78.9	<0.001
Heart failure	636,580	32.0	31.7	32.5	32.7	32.1	<0.001
Coronary disease	636,594	27.8	26.5	28.6	29.2	27.4	<0.001
Stroke	636,570	9.4	9.3	9.6	9.3	9.2	0.2
Peripheral vascular disease	636,573	15.8	14.8	15.6	16.4	16.8	<0.001
Chronic lung disease	636,568	8.9	7.9	8.9	9.6	9.4	<0.001
Malignancy	636,569	7.2	6.0	7.0	7.9	8.2	<0.001
Physical characteristics							
Height (cm) ^a	636,594	173.9 (9.6)	159.5 (7.8)	174.2 (1.3)	179 (1.2)	185.6 (3.6)	<0.001
Body mass index (kg/m ²)	633,639	26.9 (6.5)	28.4 (7.9)	26.5 (6.1)	26.4 (6.2)	26.2 (6.5)	<0.001
Weight (kg) ^a	636,594	81.1 (20.6)	71.7 (17.7)	80.3 (18.6)	84.7 (20)	90.4 (22.7)	<0.001
Lifestyle factors (%)							
Alcohol dependence	636,568	2.2	2.1	2.2	2.0	2.1	<0.48
Drug dependence	636,568	1.5	1.3	1.5	1.4	1.5	<0.001
Current smoker	636,570	6.6	5.3	6.2	6.9	7.1	<0.001
Functional status (%)							
Inability to walk independently	636,570	4.6	5.0	4.2	4.4	5.4	<0.001
Inability to transfer independently	636,569	1.9	2.2	1.7	1.8	2.2	<0.001
Employment status (%)							
Full-time employment	636,594	10.2	8.0	9.7	10.8	11.2	<0.001
Part-time employment	636,594	2.0	1.7	2.0	2.1	2.0	<0.001

Table 1. Continued

	N ^f	Q1	Q2	Q3	Q4	Q5	P value for trend
	All men (n=636,594)	<167 cm (n=118,291)	167–172 cm (n=117,543)	173–177 cm (n=140,559)	178–181 cm (n=129,553)	≥182 cm (n=130,648)	
Unemployed	636,594	18.0	21.5	17.0	15.7	15.8	<0.001
Homemaker	636,594	0.1	0.1	0.1	0.1	0.1	<0.001
Retired by age	636,594	42.1	41.6	44.2	44.2	42.8	<0.001
Retired because of disability	636,594	21.1	20.9	20.7	20.5	21.5	<0.001
Medical insurance (%)							
Medicaid	206,255	20.1	27.9	18.8	16.3	16.2	<0.001
Medicare	206,255	52.3	51.1	53.5	53.5	53.2	<0.001
Employer group health insurance	206,255	27.1	21.4	27.4	30.0	30.4	<0.001
DVA	206,255	2.9	1.8	3.3	3.4	3.6	<0.001
Medicaid advantage	206,255	4.8	5.3	4.7	4.6	4.3	<0.001
Other	206,255	23.5	21.2	24.6	24.9	24.4	<0.001
No insurance	206,255	8.5	9.5	8.2	7.6	7.8	<0.001
Laboratory variables (SD)							
Serum creatinine (mg/dl)	617,896	7.9 (3.8)	7.7 (3.7)	7.8 (3.7)	7.8 (3.7)	7.9 (4.0)	<0.001
eGFR (ml/min per 1.73m ²) ^c	617,896	8.6 (3.9)	8.6 (4)	8.6 (3.9)	8.6 (3.9)	8.6 (3.9)	<0.001
Serum albumin (mg/l)	483,637	3.2 (0.7)	3.1 (0.7)	3.2 (0.7)	3.2 (0.7)	3.2 (0.7)	<0.001
Hematocrit (%) ^a	401,485	29.6 (5.5)	29.5 (5.5)	29.7 (5.5)	29.7 (5.4)	29.6 (5.5)	<0.001
Pre-ESRD care (%) ^d							
Pre-dialysis EPO use ^d	636,288	27.6	26.2	27.4	28.7	28.2	<0.001
Under care of nephrologist	206,255	56.5	52.3	56.0	58.6	58.1	<0.001
Under care of dietitian	206,255	9.7	9.3	9.6	9.9	10.0	<0.01
Dialysis modality (%) ^e							
Peritoneal dialysis	636,472	7.4	6.0	7.5	8.2	7.7	<0.001
Hemodialysis	636,472	92.6	94.0	92.5	91.8	92.3	<0.001

^aFor all variables, apart from age, baseline characteristics are age-standardized across quintile groups using the direct method.

^bCategorical data are provided as percentage of patients and continuous data as mean±SD.

^ceGFR (ml/min per 1.73 m²) was based on the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation measured prior to dialysis onset.³⁶

^dTreatment with erythropoietin (EPO) prior to dialysis initiation was captured from 1995 to 2008. Visit with a nephrologist or dietitian prior to dialysis was recorded from 2005 onwards.

^eDialysis modality defined on the first day of chronic regular dialysis.

^fNumber of non-missing patients.

Table 2. Baseline characteristics of women by height quintiles in the US dialysis population: 1995–2008^a

	N ^f	Height Quintiles					P value for trend
		Q1 <155 cm (n=100,726)	Q2 155–159 cm (n=111,726)	Q3 160–162 cm (n=74,014)	Q4 163–167 cm (n=131,304)	Q5 ≥168 cm (n=117,478)	
Demographics							
Age (years) ^b	535,248	63.5 (15.1)	64.9 (14.8)	64 (14.8)	62.9 (14.8)	60 (15.1)	<0.001
Race (%)							
White	535,248	61.7	65.6	63	59.5	55.4	<0.001
Black	535,248	33.2	27.7	32.6	37.4	42.5	<0.001
Asian	535,248	3.9	5.1	3.0	1.9	1.1	<0.001
American Indian/Alaska native	535,248	1.3	1.6	1.4	1.2	1.0	<0.001
Hispanic (%)	533,171	11.9	16.1	11.8	8.2	4.8	<0.001
Primary cause of ESRD (%)							
Diabetes	535,248	48.7	49.3	48.8	48.6	48.1	<0.001
Hypertension	535,248	26.6	26.0	26.3	26.3	25.9	<0.001
Glomerulonephritis	535,248	7.0	7.3	7.1	7.0	7.1	<0.001
Cystic kidney disease	535,248	2.1	1.8	2.0	2.3	2.9	<0.001
Other urologic disease	535,248	1.8	1.9	1.7	1.7	1.7	<0.001
Other cause	535,248	10.3	10.2	10.6	10.7	10.9	<0.001
Unknown cause	535,248	3.5	3.5	3.5	3.4	3.3	<0.001
Comorbid conditions (%)							
Diabetes (as comorbid condition)	535,248	55.8	56.6	56.5	56.4	56.0	<0.001
Hypertension	535,241	80.6	80.5	80.7	80.6	80.9	<0.001
Heart failure	535,231	34.6	34.3	34.6	34.1	33.7	<0.001
Coronary disease	535,248	23.5	24.0	23.4	23.1	22.0	<0.37
Stroke	535,225	9.8	9.5	9.7	9.9	10.0	<0.001
Peripheral vascular disease	535,227	13.3	13.0	13.3	13.1	13.8	<0.001
Chronic lung disease	535,225	7.3	7.2	7.4	7.3	7.3	<0.001
Malignancy	535,221	5.4	5.1	5.8	5.4	5.7	<0.001
Physical characteristics							
Height (cm) ^a	535,248	160.6 (8.6)	156.6 (1.2)	160.2 (0.6)	164 (1.3)	171.2 (4.2)	<0.001
Body mass index (kg/m ²)	534,953	28.2 (8.1)	28.2 (7.9)	28.2 (7.9)	27.9 (7.8)	27.6 (7.9)	<0.001
Weight (kg) ^a	535,248	72.7 (21.6)	69.1 (19.4)	72.4 (20.3)	75.1 (21.1)	80.7 (23.4)	<0.001
Lifestyle factors (%)							
Alcohol dependence	535,221	0.7	0.7	0.7	0.8	0.7	<0.001
Drug dependence	535,221	0.7	0.7	0.7	0.8	0.9	<0.001
Current smoker	535,223	4.4	4.3	4.4	4.7	5.1	<0.001
Functional status (%)							
Inability to walk independently	535,223	5.8	5.2	5.5	5.8	6.5	<0.001

Table 2. Continued

	N ^f						P value for trend
	All Women (n=535,248)	Q1 <155 cm (n=100,726)	Q2 155–159 cm (n=111,726)	Q3 160–162 cm (n=74,014)	Q4 163–167 cm (n=131,304)	Q5 ≥168 cm (n=117,478)	
Inability to transfer independently	535,222	2.4	2.1	2.3	2.5	2.8	<0.001
Employment status (%)							
Full-time employment	535,248	4.7	5.5	5.8	6.3	6.9	<0.001
Part-time employment	535,248	1.4	1.6	1.6	1.6	1.7	<0.001
Unemployed	535,248	24.1	22.1	21.9	21.9	21.8	<0.001
Homemaker	535,248	12.3	11.7	10.5	9.6	8.5	<0.001
Retired by age	535,248	37.2	36.3	36.4	36.3	35.6	<0.001
Retired because of disability	535,248	17.4	17.1	17.7	18.0	19.1	<0.001
Medical insurance (%)							
Medicaid	163,902	36.9	32.4	30.5	30.5	30.5	<0.001
Medicare	163,902	51.9	52.7	53.7	53.9	53.9	<0.001
Employer group health insurance	163,902	19.6	22.6	24.0	24.7	25.8	<0.001
DVA	163,902	0.3	0.3	0.3	0.4	0.4	<0.001
Medicaid advantage	163,902	4.8	4.9	4.8	4.4	4.2	>0.52
Other	163,902	22.4	22.0	22.6	22.2	21.0	0.001
No insurance	163,902	6.5	7.0	6.8	6.5	6.3	<0.001
Laboratory variables (SD)							
Serum creatinine (mg/dl)	504,093	6.6 (2.9)	6.7 (3)	6.7 (3.1)	6.8 (3.1)	6.9 (3.3)	<0.001
eGFR (ml/min per 1.73m ²) ^c	504,093	7.7 (3.2)	7.7 (3.2)	7.7 (3.3)	7.6 (3.3)	7.6 (3.3)	<0.001
Serum albumin (mg/l)	404,866	3.1 (0.7)	3.1 (0.7)	3.1 (0.7)	3.1 (0.7)	3.1 (0.7)	>0.60
Hematocrit (%) ^a	346,361	29.3 (5.4)	29.4 (5.4)	29.2 (5.4)	29.2 (5.3)	29.1 (5.3)	<0.001
Pre-ESRD care (%) ^d							
Pre-dialysis EPO use ^d	535,031	30.0	31.2	30.8	30.6	30.8	<0.001
Under care of nephrologist	163,902	57.0	57.9	57.6	57.1	56.9	>0.73
Under care of dietitian	163,902	8.9	9.4	9.1	8.8	8.4	>0.002
Dialysis modality (%) ^e							
Peritoneal dialysis	535,191	7.6	8.2	7.9	7.8	7.7	<0.001
Hemodialysis	535,191	92.4	91.8	92.1	92.2	92.2	<0.001

^aFor all variables, apart from age, baseline characteristics are age-standardized across quintile groups using the direct method.

^bCategorical data are provided as percentage of patients and continuous data as mean±SD.

^ceGFR (ml/min per 1.73 m²) was based on the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation measured prior to dialysis onset.³⁶

^dTreatment with erythropoietin (EPO) prior to dialysis initiation was captured from 1995 to 2008. Visit with a nephrologist or dietitian prior to dialysis was recorded from 2005 onwards.

^eDialysis modality defined on the first day of chronic regular dialysis.

^fNumber of non-missing patients.

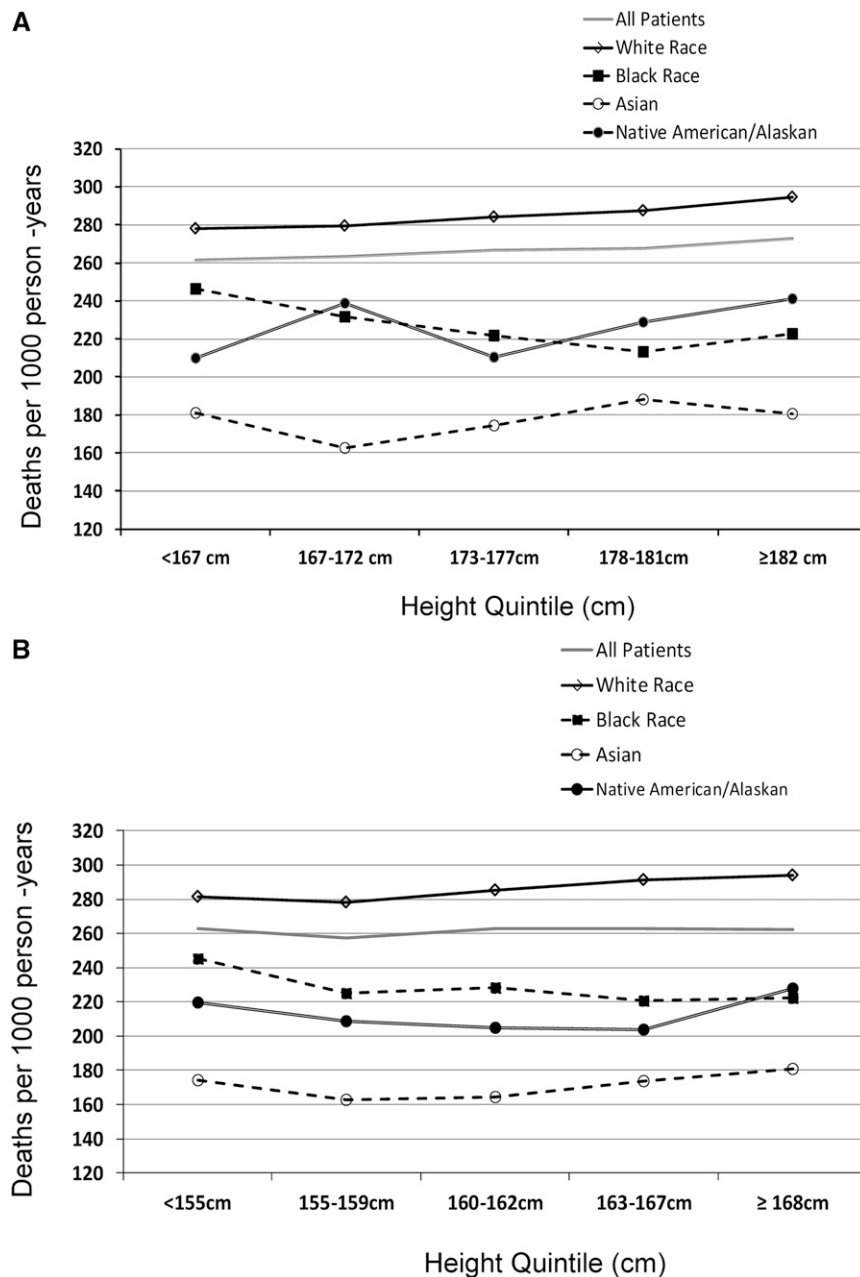


Figure 2. Age-adjusted mortality rates for (A) men and (B) women by race group across height quintiles in the United States ESRD population. $P < 0.001$ for all group comparisons.

1.06; 95% confidence interval [95% CI], 1.05–1.07) compared with the referent (Q1 <167 cm; HR=1.00). With additional adjustment for baseline characteristics, the HR was virtually unchanged. When weight was included as a covariate in the model, the magnitude of risk associated with increasing height quintile was greatly magnified especially for those in the highest quintile group (HR, 1.18; 95% CI, 1.16–1.20).

The relationship between height and mortality varied significantly across race groups (P value for interaction < 0.001) and the HR for each race subgroup is described in

Table 3. The corresponding smoothed spline hazard functions are illustrated in Figures 3A–D. The height-mortality relationships were positive and strongest for white men, American Indians/Alaska natives and Asian men as illustrated. In each of these analyses, the extended model with adjustment for the weight covariate resulted in significantly higher HR for death. For black men, however, the pattern was significantly different. Both in the unadjusted and the multivariate adjusted model, increasing height was associated with significantly lower mortality (HR, 0.91; 95% CI, 0.88–0.94 for the highest quintile versus the referent). When weight was added to the model, the HR only changed marginally and became positive only for the highest quintile group.

The age-adjusted and multivariable-adjusted HRs for death with increasing quintile of height are shown for women in Table 4 and Figures 3A–D. In general these associations paralleled those observed in men, although the associations were much weaker and not all were statistically significant. Again evidence of significant heterogeneity was present across race groups with white women showing a positive association, while black women showed an inverse association.

The robustness of our observations was confirmed in several sensitivity analyses. First, we stratified the cohort by dialysis modality and examined associations of height with mortality separately for hemodialysis (HD) and peritoneal dialysis (PD). In these series of analysis, increasing height was associated with elevated mortality for both dialysis subgroups, although the pattern was accentuated in HD (Supplemental Table 1). Within HD, we specifically examined whether the association of height with mortality was influenced by the number of treatment hours of dialysis prescribed per week. In contrast, we found that taller patients were more likely to receive longer treatment times but the pattern of higher mortality with increasing height persisted irrespective of whether patients were prescribed exactly 9 hours or exactly 12 hours treatment per week (Supplemental Table 2). The duration of the treatment did influence the height-mortality association and was more marked among patients who had received shorter treatments ($P < 0.01$ for interaction). Second, neither vascular access type nor the duration of predialysis nephrology care modified the association of height with

Table 3. Unadjusted and multivariable adjusted HRs for death among men by height quintile stratified by race

	Quintile group					
	Continuous (per 5 cm increase)	Q1 <167 cm	Q2 167–172 cm	Q3 173–177 cm	Q4 178–181 cm	Q5 ≥182 cm
	HR (95% CI) ^a	Referent quintile	HR (95% CI) ^a	HR (95% CI) ^a	HR (95% CI) ^a	HR (95% CI) ^a
Overall						
Age adjusted	1.00 (1.00–1.01)	1.00	1.00 (0.99–1.02)	1.02 (1.01–1.04)	1.03 (1.02–1.04)	1.06 (1.05–1.07)
Multivariate adjusted ^b	1.00 (1.00–1.01)	1.00	1.01 (0.99–1.02)	1.02 (1.00–1.03)	1.03 (1.01–1.04)	1.04 (1.03–1.06)
Plus weight ^c	1.02 (1.02–1.03)	1.00	1.04 (1.02–1.06)	1.08 (1.06–1.10)	1.12 (1.10–1.14)	1.18 (1.16–1.20)
Plus dietitian visit ^d	1.02 (1.02–1.03)	1.00	1.03 (1.01–1.06)	1.07 (1.05–1.10)	1.11 (1.08–1.14)	1.16 (1.13–1.20)
Plus nephrology visit ^d	1.02 (1.02–1.03)	1.00	1.04 (1.01–1.07)	1.08 (1.05–1.11)	1.12 (1.09–1.15)	1.17 (1.14–1.20)
White						
Age adjusted	1.01 (1.01–1.01)	1.00	1.00 (0.99–1.02)	1.02 (1.01–1.04)	1.04 (1.03–1.06)	1.08 (1.07–1.10)
Multivariate adjusted ^b	1.01 (1.01–1.01)	1.00	1.01 (0.99–1.02)	1.03 (1.01–1.04)	1.05 (1.03–1.06)	1.07 (1.05–1.09)
Plus weight ^c	1.03 (1.02–1.03)	1.00	1.03 (1.02–1.05)	1.08 (1.06–1.10)	1.13 (1.11–1.15)	1.19 (1.17–1.22)
Plus dietitian visit ^d	1.03 (1.02–1.04)	1.00	1.03 (1.00–1.06)	1.07 (1.04–1.11)	1.12 (1.09–1.16)	1.20 (1.16–1.24)
Plus nephrology visit ^d	1.03 (1.02–1.04)	1.00	1.03 (1.00–1.07)	1.08 (1.05–1.11)	1.13 (1.10–1.17)	1.21 (1.17–1.25)
Black						
Age adjusted	0.97 (0.97–0.98)	1.00	0.94 (0.91–0.96)	0.90 (0.87–0.92)	0.85 (0.82–0.87)	0.87 (0.85–0.89)
Multivariate adjusted ^b	0.98 (0.98–0.99)	1.00	0.97 (0.94–1.00)	0.93 (0.90–0.96)	0.89 (0.86–0.92)	0.91 (0.88–0.94)
Plus weight ^c	1.00 (1.00–1.01)	1.00	0.99 (0.96–1.03)	0.99 (0.96–1.02)	0.99 (0.96–1.02)	1.06 (1.02–1.09)
Plus dietitian visit ^d	1.00 (0.99–1.01)	1.00	0.99 (0.93–1.05)	0.99 (0.93–1.05)	0.98 (0.92–1.04)	1.02 (0.96–1.08)
Plus nephrology visit ^d	1.00 (0.99–1.01)	1.00	0.99 (0.93–1.05)	0.99 (0.94–1.05)	0.98 (0.93–1.05)	1.02 (0.96–1.08)
Asian						
Age adjusted	0.98 (0.97–0.99)	1.00	0.92 (0.87–0.98)	1.02 (0.94–1.09)	1.03 (0.93–1.15)	1.10 (0.95–1.26)
Multivariate adjusted ^b	0.98 (0.97–1.00)	1.00	0.94 (0.88–1.01)	1.02 (0.93–1.11)	1.01 (0.90–1.15)	1.01 (0.85–1.19)
Plus weight ^c	1.00 (0.99–1.02)	1.00	1.00 (0.93–1.07)	1.12 (1.03–1.23)	1.17 (1.03–1.33)	1.22 (1.03–1.45)
Plus dietitian visit ^d	0.99 (0.96–1.02)	1.00	1.00 (0.89–1.13)	1.12 (0.97–1.30)	1.22 (0.99–1.50)	1.07 (0.79–1.43)
Plus nephrology visit ^d	0.99 (0.96–1.01)	1.00	1.00 (0.88–1.12)	1.12 (0.96–1.30)	1.21 (0.98–1.49)	1.06 (0.79–1.42)
American Indian/Alaska native						
Age adjusted	1.01 (0.99–1.04)	1.00	1.07 (0.92–1.24)	1.00 (0.87–1.15)	1.08 (0.93–1.25)	1.12 (0.96–1.31)
Multivariate adjusted ^b	1.02 (0.99–1.05)	1.00	1.18 (1.00–1.39)	1.10 (0.93–1.29)	1.12 (0.95–1.33)	1.17 (0.98–1.39)
Plus weight ^c	1.04 (1.01–1.08)	1.00	1.20 (1.02–1.42)	1.15 (0.97–1.35)	1.21 (1.01–1.44)	1.28 (1.07–1.54)
Plus dietitian visit ^d	0.98 (0.93–1.03)	1.00	1.03 (0.77–1.37)	0.92 (0.69–1.22)	1.01 (0.75–1.37)	0.84 (0.60–1.17)
Plus nephrology visit ^d	0.98 (0.93–1.03)	1.00	1.06 (0.80–1.41)	0.92 (0.70–1.23)	1.03 (0.76–1.39)	0.85 (0.61–1.18)

CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration.

^aHRs and 95% CIs.^bMultivariable model adjusted for: age, cause of end-stage kidney disease, co-morbid conditions at time of dialysis initiation (coronary artery disease, peripheral vascular disease, heart failure, stroke, hypertension, diabetes, chronic lung disease, and malignancy), lifestyle factors (current smoker status, drug and alcohol addiction), functional status indicators (inability to ambulate, inability to transfer independently), socioeconomic factors (employment status, insurance status at time of dialysis), baseline eGFR (from the CKD-EPI equation), albumin, and use of erythropoietin prior to dialysis initiation, incident year of cohort.^cBody weight measured prior to first dialysis treatment was included in extended model to account for differences in body size.^dVisit with a nephrologist or dietitian was substituted for pre-dialysis erythropoietin in extended models to account for differences in care patterns prior to dialysis initiation.

mortality. Third, we imputed missing data for explanatory variables used in the adjusted models for the 636,594 men and 535,248 women. This analysis yielded results that were virtually identical to the original (Supplemental Table 3). Fourth, we evaluated the impact of dialysis vintage on the height-mortality relationship by recalculating the HR among survivors at 1, 2, and 3 years after dialysis initiation. Again, in these series of analyses, the pattern of mortality with increasing height was virtually unchanged (Supplemental Table 4) and persisted after 5-year follow-up (Supplemental Tables 5 and 6). Finally, in a series of further analyses, where we excluded kidney transplantation as a censoring variable, the general pattern of elevated mortality with increasing tallness persisted.

DISCUSSION

The findings from this large representative study of United States dialysis patients demonstrate that increasing adult height is directly and independently associated with mortality. This association of tallness with elevated mortality was present for both men and women who began dialysis treatment although the relationship was generally weaker in women. Our analyses uncovered an important effect modification of race on the height-mortality risk association. Increasing height was directly associated with higher mortality risks for whites, Asians and American Indians/Alaska natives with the exception of black men and black women, where height was inversely

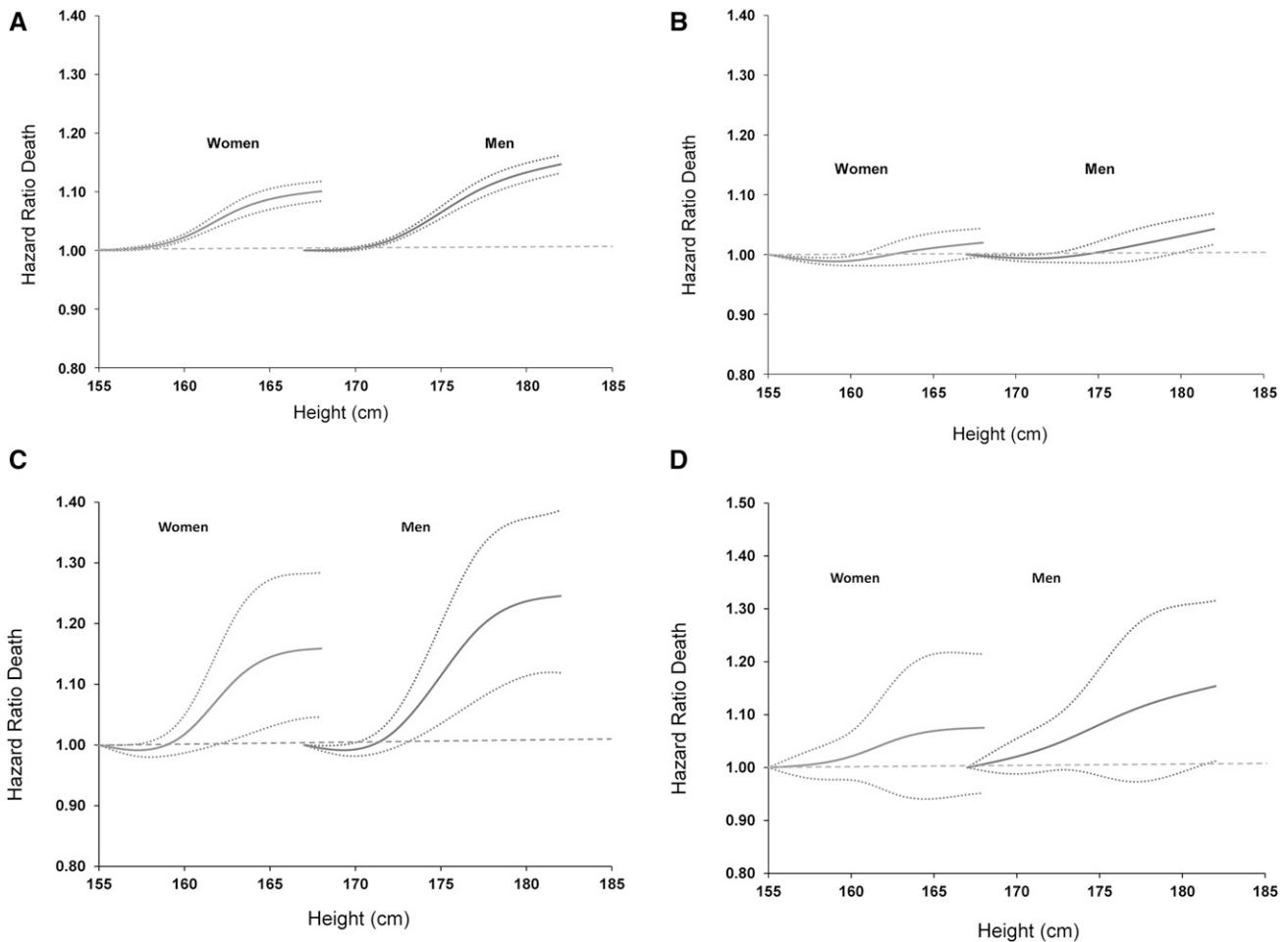


Figure 3. Association of height with hazard ratio of death by race group for men and for women. Height mortality relationships for (A) whites, (B) blacks, (C) Asians, and (D) American Indians/Alaska natives. Height was modeled by a restricted cubic spline with four knots placed at the 20th, 40th, 60th and 80th percentiles of height for men and women, respectively. Models are adjusted for age, cause of ESRD, comorbid conditions at time of dialysis (coronary artery disease, peripheral vascular disease, heart failure, stroke, hypertension, diabetes, chronic lung disease, and malignancy), lifestyle factors (smoking status, drug and alcohol addiction), functional status indicators (inability to ambulate, inability to transfer independently), socioeconomic factors (employment status, insurance status at time of dialysis), baseline eGFR (from the CKD-EPI equation), albumin, use of erythropoietin prior to dialysis initiation, and incident year of cohort. HRs with 95% CI in dotted lines. CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration.

related to mortality. The observations from this study contrast with findings from the general population and show for the first time that tallness does not contribute to greater life expectancy for the majority of patients who reach ESRD.

The present study sheds new light on the patterns of association of height with mortality among men and women who develop ESRD. Although studies in the general population have suggested that the benefit associated with tallness is uniformly positive,^{6–9} this study has found the contrary. Taller patients did not achieve greater lifespans than shorter patients. We had speculated that this new finding may well reflect the fact that taller persons with advanced kidney disease had accumulated a greater burden of illness during the predialysis period prior to dialysis initiation. Indeed, comparisons of quintile groups at baseline found higher prevalence of several

chronic diseases including chronic lung disease, peripheral vascular disease, and malignancy in taller compared with shorter individuals. Yet when we accounted for these baseline differences in the multivariable models, the pattern of association of height with elevated mortality was virtually unchanged.

To assess fully the independence of this new association of height with elevated mortality, we carefully considered several situations where patient-level or treatment-level factors may have confounded the relationship. When we stratified by dialysis modality, we found that the relationship of height with mortality for patients undergoing HD was similar to those of the original analysis. The pattern was identical even when accounting for vascular access type. Furthermore, when we evaluated the relationship of height with mortality according

Table 4. Unadjusted and multivariable adjusted HRs for death among women by height quintile stratified by race

	Quintile group					
	Continuous (per 5 cm increase)	Q1 <155 cm	Q2 155–159 cm	Q3 160–162 cm	Q4 163–167 cm	Q5 ≥168 cm
	HR (95% CI)	Referent quintile	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)
Overall						
Age adjusted	1.00 (1.00–1.01)	1.00	0.99 (0.98–1.01)	1.02 (1.00–1.03)	1.02 (1.01–1.03)	1.03 (1.01–1.04)
Multivariate adjusted ^b	1.00 (1.00–1.00)	1.00	0.98 (0.97–1.00)	1.01 (0.99–1.03)	1.00 (0.99–1.02)	1.00 (0.99–1.02)
Plus weight ^c	1.01 (1.01–1.02)	1.00	1.00 (0.99–1.02)	1.05 (1.03–1.06)	1.05 (1.03–1.07)	1.08 (1.06–1.10)
Plus dietitian visit ^d	1.02 (1.01,1.02)	1.00	1.02 (0.99–1.05)	1.06 (1.02–1.09)	1.07 (1.04–1.11)	1.09 (1.06–1.13)
Plus nephrology visit ^d	1.02 (1.01,1.02)	1.00	1.02 (0.99–1.05)	1.06 (1.02–1.09)	1.07 (1.04–1.11)	1.09 (1.06–1.13)
White						
Age adjusted	1.01 (1.01–1.02)	1.00	1.00 (0.99–1.02)	1.03 (1.01–1.05)	1.05 (1.04–1.07)	1.08 (1.06–1.10)
Multivariate adjusted ^b	1.01 (1.01–1.02)	1.00	1.00 (0.98–1.02)	1.03 (1.01–1.05)	1.04 (1.02–1.06)	1.06 (1.04–1.08)
Plus weight ^c	1.02 (1.02–1.03)	1.00	1.02 (1.00–1.04)	1.06 (1.04–1.08)	1.08 (1.06–1.10)	1.12 (1.10–1.15)
Plus dietitian visit ^d	1.03 (1.02,1.03)	1.00	1.02 (0.99–1.06)	1.07 (1.03–1.12)	1.11 (1.07–1.15)	1.14 (1.09–1.18)
Plus nephrology visit ^d	1.03 (1.02,1.03)	1.00	1.03 (0.99–1.06)	1.07 (1.03–1.12)	1.11 (1.07–1.15)	1.14 (1.09–1.18)
Black						
Age adjusted	0.98 (0.98–0.98)	1.00	0.92 (0.89–0.95)	0.92 (0.90–0.95)	0.90 (0.88–0.92)	0.90 (0.87–0.92)
Multivariate adjusted ^b	0.98 (0.98–0.99)	1.00	0.92 (0.89–0.95)	0.95 (0.91–0.98)	0.91 (0.89–0.94)	0.91 (0.88–0.93)
Plus weight ^c	1.00 (0.99–1.00)	1.00	0.94 (0.91–0.97)	0.98 (0.95–1.02)	0.96 (0.93–0.99)	0.99 (0.96–1.02)
Plus dietitian visit ^d	1.00 (0.99–1.01)	1.00	0.94 (0.88–1.00)	0.98 (0.92–1.05)	0.97 (0.92–1.03)	0.99 (0.93–1.05)
Plus nephrology visit ^d	1.00 (0.99–1.01)	1.00	0.94 (0.89–1.00)	0.98 (0.92–1.05)	0.97 (0.91–1.03)	0.98 (0.93–1.04)
Asian						
Age adjusted	1.00 (0.98–1.01)	1.00	0.96 (0.90–1.02)	0.99 (0.9–1.08)	1.06 (0.97–1.16)	1.09 (0.97–1.22)
Multivariate adjusted ^b	0.99 (0.97–1.01)	1.00	0.94 (0.88–1.02)	0.97 (0.87–1.08)	1.01 (0.91–1.12)	1.04 (0.91–1.20)
Plus weight ^c	1.00 (0.98–1.02)	1.00	0.97 (0.90–1.04)	1.01 (0.90–1.12)	1.07 (0.96–1.19)	1.14 (0.99–1.31)
Plus dietitian visit ^d	1.02 (0.93–1.05)	1.00	1.02 (0.89–1.17)	0.97 (0.80–1.18)	1.09 (0.90–1.32)	1.27 (0.99–1.63)
Plus nephrology visit ^d	1.02 (0.98–1.06)	1.00	1.02 (0.89–1.17)	0.97 (0.80–1.17)	1.09 (0.90–1.32)	1.27 (0.98–1.63)
American Indian/Alaska native						
Age adjusted	1.02 (0.99–1.04)	1.00	0.93 (0.82–1.05)	0.91 (0.78–1.05)	0.99 (0.87–1.13)	1.08 (0.94–1.25)
Multivariate adjusted ^b	1.00 (0.97–1.03)	1.00	0.93 (0.81–1.08)	0.90 (0.76–1.07)	0.95 (0.82–1.11)	1.00 (0.85–1.17)
Plus weight ^d	1.02 (0.98–1.05)	1.00	0.96 (0.83–1.11)	0.93 (0.78–1.1)	1.00 (0.86–1.16)	1.08 (0.91–1.28)
Plus dietitian visit ^d	1.05 (0.99–1.12)	1.00	1.01 (0.76–1.34)	0.86 (0.62–1.2)	1.00 (0.74–1.36)	1.27 (0.92–1.76)
Plus nephrology visit ^d	1.05 (0.98–1.12)	1.00	1.01 (0.76–1.34)	0.88 (0.63–1.2)	1.00 (0.74–1.35)	1.26 (0.92–1.74)

CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration.

^aHRs and 95% CIs.^bMultivariable model adjusted for: age, cause of end stage kidney disease, comorbid conditions recorded at time of dialysis initiation (coronary artery disease, peripheral vascular disease, heart failure, stroke, hypertension, diabetes, chronic lung disease, and malignancy), lifestyle factors (current smoker, drug and alcohol addiction), functional status indicators (inability to ambulate, inability to transfer independently), socioeconomic factors (employment status, insurance status at time of dialysis), baseline eGFR (from the CKD-EPI equation), albumin, and use of erythropoietin prior to dialysis initiation, incident year of cohort.^cBody weight measured prior to first dialysis treatment was included in extended model to account for differences in body size.^dVisit with a nephrologist or dietitian was substituted for pre-dialysis erythropoietin use in extended models to account for differences in care patterns prior to dialysis initiation.

to the duration of dialysis prescribed per week, we found that taller individuals experienced significantly higher mortality risks irrespective of whether they received 9 hours or 12 hours of treatment, although the risks were accentuated for those who were prescribed shorter treatment times. For patients treated with PD, the patterns of association with mortality were similar to HD but far more striking in men than in women. These findings would suggest that the relationship of height with mortality is independent of the treatment strategy including the number of hours prescribed per week.

Prior studies have demonstrated that differences in the delivery of care prior to the onset of dialysis may influence patient survival following dialysis initiation.^{26,27} We carefully

examined whether the association of height with mortality might have been influenced by differential access to nephrology care or the duration of care prior to dialysis initiation. Our analysis revealed that greater proportions of taller patients received care from a nephrologist or dietitian in the period preceding dialysis initiation. As before, when we adjusted for these differences in predialysis care patterns, the results were visibly unchanged. We also considered the possibility that missing data on important explanatory covariates might have altered our results; however, our multiple imputation strategy for missingness gave rise to similar findings. Finally, we demonstrated that the pattern of mortality risk was consistent among survivor cohorts at 1 year, 2 years, and up to

3 years after dialysis initiation. These observations would suggest that the prognostic importance of height on mortality is independent of baseline health at dialysis initiation and associated care delivery practices provided prior to dialysis initiation.

An interesting but perplexing finding was the divergent risk associations of race on the height-mortality association. The strong interaction between race and height with mortality was present for men and women, and in each case tallness among blacks was inversely associated with all-cause mortality. The reasons for these differences between blacks and whites are unknown. As final adult height is largely determined by both genetic and environmental factors,¹ we surmised that differences in the distribution of these factors between black and non-blacks may account for these differences. We found that black men and women, compared with their white counterparts, were younger in age and had a lower prevalence of diabetes, coronary disease, and heart failure, factors that may have given them a favorable survival advantage. Taller individuals had better socioeconomic circumstances with higher proportions in employment, in receipt of health insurance and predialysis care. Although white and black patients should benefit equally from these socioeconomic supports, it is possible that black patients benefited proportionally more from these factors at dialysis initiation. Given that height is a polygenic trait with up to 90% heritability, it is equally plausible that genes associated with height may exhibit different effects in blacks compared with whites.²⁸ In support of this hypothesis, studies comparing blacks with whites have found significantly greater bone mineral density, bone mineral content, skeletal weight, and body protein content in blacks than in whites, adjusting for weight, height and age.²⁹

A striking feature of the current study is the loss of survival benefit for tall white patients, findings that contrast with the general United States population. Prospective cohort studies of white men and women have convincingly shown that taller individuals experience lower death risks from all causes.⁶⁻⁹ Paradoxically, tallness among white patients undergoing dialysis appears to be an adverse risk marker, compared with the general white population. These seemingly discordant findings may well represent a reverse epidemiologic finding that is commonly observed with certain cardiovascular risk factors in ESRD.³⁰⁻³² In this scenario, factors which are usually associated with positive effects on survival exhibit deleterious effects in specific populations with chronic conditions. It is also possible that the adverse impact of height on mortality among whites may be partly related to higher cancer mortality rates.^{13,15} The Emerging Risk Factors Collaboration study found a 4% increase in cancer mortality risk for men and a 5% increase for women with each 6.5 cm increase in height.¹⁵

This study is not without limitations. Height measurements were self-reported and the exact timing of measurements for patients was not available although physicians were instructed to record the most recent height measurement prior to first dialysis. While an extensive list of comorbid conditions is

captured from the Medical Evidence Form, the severity of disease was not available. We also accept that this study, while representative of the United States dialysis population may not represent patients from countries outside the United States. Although our analyses captured data on the duration of dialysis treatments in HD, we lacked information on dialysis dose, an important determinant of survival from prior studies.^{33,34} It is also possible that residual bias may influence our results due to unmeasured or imprecisely measured confounders. The limitations of this study were counterbalanced by several strengths. The large sample size of over 1 million patients provided a powerful mechanism to examine for effect modification and test hypotheses in several subgroups. Mandatory participation in the United States registry ensures that our results are generalizable to the entire United States dialysis population. The USRD captured data on multiple confounders including comorbid disease, laboratory variables, socioeconomic factors, and care delivery patterns allowing us to examine in great detail the independence of the height-mortality relationship. The availability of data on body weight prior to dialysis initiation provided us with an additional opportunity to account for the influence of weight in the height-mortality relationship.

In this population based study of over 1 million new dialysis patients, we observed a strong independent association of height with elevated mortality. This finding was present for men and for women and most race groups except blacks where the association was inversely related with mortality. This relationship was not explained by prevailing burden of medical illness, differences in socioeconomic factors or care practices prior to or after dialysis initiation. Contrary to findings in the general population, there was no overall survival benefit of tallness over shortness in the majority of patients who reach ESRD.

CONCISE METHODS

The study population represented a historical prospective cohort of 1,171,842 United States patients, who began dialysis between May 1, 1995 and December 31, 2008, and had follow-up until December 31, 2010. Data sufficient for these analyses were obtained from merged standard analysis files (SAFs) of the USRD.¹³ The Medical Evidence SAF is derived from the Center for Medicare and Medicaid Services (CMS) Medical Evidence Form, a government document that is completed for all new patients initiated on dialysis.³⁵ The CMS form captures data on demographic characteristics, anthropometric measures, comorbid conditions, measures of functional status, laboratory indices, and date and type of dialysis treatment provided for all incident patients. The form is completed by medical personnel who care for patients in each dialysis facility through data abstraction from patients' medical records. The following variables were included for our analyses: height (cm), age, gender, race (classified as white, black, Asian and American Indian/Alaska native, cause of ESRD, comorbid conditions including: diabetes, hypertension, coronary artery

disease, peripheral arterial disease, stroke, diabetes, congestive heart failure, chronic lung disease, malignancy, alcohol use, drug dependence, smoking, inability to ambulate and transfer independently, current employment status, insurance status, and measures of predialysis care. Laboratory data included hematocrit, serum albumin and creatinine measured at or prior to dialysis initiation. Residual renal function at dialysis initiation was estimated from estimated GFR using the Chronic Kidney Disease Epidemiology Collaboration.³⁶ The study had approval from the Ethics Committee at University Hospital Limerick in accordance with the Declaration of Helsinki.

Cohort Assembly

The medical evidence ($n=1,753,496$ patients) and mortality files ($n=2,377,166$ patients) were merged to create the final analytic dataset (Figure 1). After merging and removal of duplicate patients, we then excluded patients with missing or unknown race, date of first treatment before May 1995, unknown sex, cause of ESRD unknown, age <18 or >100 and medical evidence forms completed before May 1, 1995. This left us with 1,445,980 patients. Next, we excluded patients with missing height or weight ($n=51,538$) and finally patients where the date of first treatment was post December 2008 ($n=222,600$). There were 1,171,842 patients in the final study cohort.

Height Measurements for Men and Women

Height was recorded at the beginning of dialysis treatment for all patients and categorized in sex-specific quintiles (Q). For men the height quintiles were: Q1 <167 cm, Q2 167–172 cm, Q3 173–177 cm, Q4 178–181 cm, and Q5 ≥ 182 cm. For women, the corresponding quintiles were: Q1 <155 cm, Q2 155–159 cm, Q3 160–162 cm, Q4 163–167 cm, and Q5 ≥ 168 cm. These ten categories allowed a detailed examination of the association between height and mortality across a wide range of height values without prior assumptions regarding the shape of any dose–response curve.

Mortality Assessment

Mortality data were derived from two sources, the CMS death notification form and the Social Security Administration's death master file.¹³ Together these provide the date and cause of death for all patients who received renal replacement therapy in the United States. Death from all causes was the primary end point for all analyses.

Statistical Analysis

Age-adjusted baseline characteristics according to each height quintile were obtained for men and for women using direct standardization. The reference population was the entire cohort of 1,171,842 patients who began dialysis treatment between May 1995 and December 2008. Multiple linear regression and logistic regression models were used to test for linear trends in height, adjusting for age.

Two-year mortality rates were calculated for each race and sex group as the number of death events divided by person-time of follow-up. Mortality rates were age adjusted using direct standardization. Cox regression models were used to describe the relationship between height quintile and mortality adjusting for age, race, cause of ESRD, comorbid conditions, laboratory variables, lifestyle indicators, and socioeconomic measures. In addition, we adjusted for the weight of patients recorded prior to first

dialysis to account for its prognostic impact on mortality. Multivariate adjusted HRs for each height quintile (using the first quintile as referent) and associated 95% CIs were determined. By adding an interaction term between height quintile and race, we found that the effect of height on mortality varied significantly by race group ($P<0.001$) among men and among women. For this reason, the final analyses were stratified by race. The functional relationship between height and death was further examined in a series of restricted cubic spline functions with four knots placed at the 20th, 40th, 60th, and 80th percentiles of height for men and women, respectively. The proportional hazards assumption was checked by including a survival time \times height quintile interaction in the full model. The primary analyses were conducted using non-missing data on all covariates using SAS v9.3 software (SAS Institute, Inc., Cary, NC).

Sensitivity Analysis

We conducted a series of carefully constructed additional analyses to evaluate the robustness of our results. First, we examined whether the association of height with mortality differed by dialysis modality (HD and PD), and by the number of hours of dialysis prescribed per week, as taller patients may preferentially have been directed toward a particular modality and prescribed longer treatments. Second, we further explored whether our findings differed by the presence and duration of predialysis nephrology care and by vascular access type at dialysis initiation. Third, to account for possible bias due to different missing data patterns across height quintiles, we imputed missing covariate data for the 636,594 men and 535,248 women in Tables 1 and 2 and repeated the original analyses. Missing covariate information was imputed by first estimating a joint multivariate normal distribution for all covariates and then simulating missing covariates from the appropriate conditional distributions. Identical multivariate models were fitted to three independently imputed datasets. In each case, the log HRs and associated standard errors were combined using the SAS procedure MIanalyze to produce a single log HR and standard error for each model. Fourth, we assessed whether the relationships observed differed by different dialysis vintage by repeating the analyses at intervals of 1, 2, 3, and 4 years. We also extended follow-up to 5 years to assess the association of height on long-term mortality. Fifth, we removed kidney transplantation as a censoring variable as we surmised that patient height may be correlated with the risk of transplantation thereby creating a potential survival bias. Finally, we assessed the external validity of our results to that of the general United States dialysis population by comparing individuals who were excluded at baseline with those who were included in the final analysis.

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DISCLOSURES

Dr. Stack had full access to all of the data in the study and takes responsibility for the integrity of the data and analysis. All authors collaborated on the study design, analysis, editing and final manuscript. The results presented in this paper have not been published previously in whole or part, except in abstract format. Dr. Stack has consulted for Amgen, Abbott and AstraZeneca and has an investigator-initiated grant from Abbott. The other authors have no relevant financial relationships to disclose.

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