Ethnic differences in survival on dialysis in Europe

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ABSTRACT

Background In Western countries, black and Asian dialysis patients experience better survival compared with white patients. It is currently unknown whether – in Western countries – patients originating from other Western countries have differential survival rates compared with native patients. Moreover, it is unknown whether duration of residence in the immigration country before the initiation of dialysis is associated with mortality on dialysis.

Methods We analyzed survival data of incident chronic dialysis patients in Denmark (1995-2010). We determined the association of (1) region of origin with mortality and (2) duration of residence in Denmark with mortality using Cox regression analysis. Hazard Ratios (HRs) for mortality were adjusted for socio-demographic and clinical characteristics.

Results Of 9,109 patients, 8,459 were native Danes; 344 originated from other Western countries; 79 from North Africa or West Asia; 173 from South or South-East Asia; and 54 from Sub-Saharan Africa. Native Danes had greater HRs for mortality compared with these groups (adjusted HRs for mortality (95% CI): 1.32 (1.14-1.54); 2.22 (1.51-3.23); 1.79 (1.41-2.27); 2.00 (1.10-3.57), respectively). Compared with immigrants living in Denmark for >20 years, the adjusted HRs for mortality (95% CI) for immigrants living in Denmark for >10-≤20 years and ≤10 years were 0.71 (0.51-0.98) and 0.64 (0.44-0.94), respectively.

Conclusion In Denmark, incident chronic dialysis patients originating from countries other than Denmark have a better survival compared with native Danes. This survival advantage becomes smaller with increased duration of residence in Denmark. Our results suggest that migration and environmental factors play a role in ethnic differences in survival on dialysis.

INTRODUCTION

In 1987, Held et al. described that while on dialysis treatment black Americans had a lower risk of death than non-black Americans.[1] Since then, studies have consistently reported ethnic differences in survival on dialysis treatment.[2-13] These studies demonstrated that black and Asian patients on chronic dialysis treatment in Western countries experience better survival compared with their white counterparts. Although extensively studied, the exact reasons for ethnic survival disparities on dialysis are far from understood.[14;15]

In most studies on ethnic differences in survival on dialysis, data on country of origin and duration of residence in the immigration country are not available.[2-13;16] Hence, it is currently unknown whether – in Western countries – patients originating from other Western countries have differential survival rates compared with native dialysis patients. Moreover, it is unknown whether duration of residence in the immigration country before the initiation of dialysis is associated with mortality on dialysis. These data, however, are important as they provide further insights into possible explanations for ethnic differences in survival on dialysis. For example, if patients originating from other Western countries have differential survival rates compared with native dialysis patients in those countries, this may imply that migration factors could contribute to ethnic differences in survival on dialysis. Furthermore, if an increased duration of residence in the immigration country before the initiation of dialysis is associated with a mortality risk similar to that of the native dialysis population, this may imply that environmental factors contribute to ethnic differences in survival on dialysis.

In the present study within the group of patients starting dialysis in Denmark, we compared the survival of native Danish patients with that of patients originating from other countries, including Western countries. Also, we explored whether duration of residence in Denmark before the start of dialysis is associated with mortality on dialysis.

METHODS

Study cohort

The main data source of this study was the Danish Nephrology Registry (DNR). Details on the DNR have been previously published.[17] In short, the DNR is a clinical database that contains data on all end-stage renal disease (ESRD) patients treated with renal replacement therapy in Denmark from 1 January 1990. All Danish dialysis centers extract data from medical records and transfer these to the DNR. Besides, we used data of other Danish Registries, including Statistics Denmark[18], the Danish Civil Registration System[19], the Danish National Patient Register[20], the Danish National Prescription Registry[21;22] and the Danish Register of Causes of Death.[23] In Denmark, all citizens have a unique personal identification number assigned from birth or immigration by the Danish Civil Registration System. Researchers and official institutions can access and link individual level data from Danish registries by using these numbers.[24] For the present study, patients from the DNR were included in case they (1) started hemodialysis (HD) or peritoneal dialysis (PD) in Denmark between 1 January 1995 and 1 November 2010 as first renal replacement therapy (1995 was chosen since in 1994 many changes were made in the DNR); (2) continued dialysis treatment for at least 90 days; (3) were ≥18 years of age at initiation of dialysis treatment; and(4) had data available on country of origin.

Region of origin

A difference was made between immigrants, descendants, and native Danes. In line with Statistics Denmark, immigrants were defined as those born outside Denmark whose parents were both born outside Denmark, descendants as those born in Denmark whose parents were both born outside Denmark, and native Danes as those having at least one parent born in Denmark.[18] For all patients, country of origin was determined based on data from Statistics Denmark. For immigrants country of origin was defined as country of birth, for descendants country of origin was defined as mothers' country of birth, and for native Danes country of origin was defined as Denmark. Subsequently, the countries of origin were categorized into regions of origin using the United Nations classification system.[25] These regions of origin were used to define ethnic groups. Beside native Danes, five ethnic groups were defined: immigrants and descendants originating from (1) North America, Europe, or Oceania (Western countries); (2) North Africa or West Asia (Arabic counties); (3) South Asia or South-East Asia; (4) Sub-Saharan Africa; and (5) other regions (i.e. central and East Asia,

central and South America, Caribbean). Immigrants and descendants originating from 'other regions' were excluded from the analyses because of small numbers.

Duration of residence

Data on duration of residence were analyzed for immigrants. Duration of residence was defined as the number of years living in Denmark before the start of dialysis and was calculated based on data on immigration year obtained from Statistics Denmark (available since 1973).

Mortality

Patients were followed from day 90 after the initiation of dialysis therapy (baseline) till death or censoring. Patients were treated as censored when they (1) had a recovery of renal function; (2) emigrated from Denmark; (3) underwent a renal transplantation; or (4) reached the end of the study period at 18 February 2011. Dates of dialysis initiation, recovery of renal function, and renal transplantation were obtained from the DNR. Data on emigration were ascertained from both the Danish Civil Registration System and the DNR. Date of death was ascertained from the Danish Civil Registration System. In the Danish Civil Registration System, death certificates issued abroad were excluded due to validity problems. Data on cause of death was obtained from the DNR using ERA-EDTA codes[26] and where needed these were completed with data from the Danish Register of Causes of Death.

Covariates

Data on age, sex, initial treatment modality, and primary kidney disease were ascertained from the DNR. Primary kidney disease was classified according to the codes of the 10th edition of the WHO's International Classification of Diseases (ICD-10).[27] Household income, including transfer payments, business profits, and pensions (except for private pensions), was obtained from Statistics Denmark and corrected for inflation with 2009 as index year. Data on hospital admissions were ascertained from the Danish National Patient Registry. This administrative registry contains information on dates and ICD-10 (before 1994 ICD-8) diagnoses of hospital admissions. Hospital admissions due to cardiovascular disease were defined as admissions because of acute myocardial infarction and/or stroke. Hospital admissions for cancer were defined as admissions or outpatient contacts due to any kind of cancer excluding non-melanoma skin cancers. For each patient, the Charlson comorbidity index was calculated based on 19 different diagnoses of hospital admissions within one year before the start of dialysis. The Charlson comorbidity index is a validated method of

classifying prognostic comorbidity in longitudinal studies.[28] Data on prescribed anti-hypertensive and anti-diabetic medication were obtained from the Danish National Prescription Registry. This registry contains information on drugs prescribed and sold, except for in-hospital drug use. Data on household income, comorbidity, and medication were based on a period one year prior to the start of dialysis to prevent incorrect classification of immigrants who migrated to Denmark shortly before the start of dialysis.

Statistical analysis

Differences in patient characteristics between native Danes and other ethnic groups were analyzed with t tests, Wilcoxon signed rank sum tests, and Chi^2 tests where appropriate. Crude and age-standardized incidence rates of death, recovery of renal function, emigration, and renal transplantation were calculated for the different ethnic groups. Age-standardized incidence rates were calculated using direct standardization with the total dialysis population as standard population (age groups 18-39, 40-49, 50-59, 60-69 and 70+). Competing risk analysis was used to calculate cumulative incidence curves for mortality for the different ethnic groups, taking account of renal transplantation as a competing end point.[29] Cox proportional hazards analysis was used to estimate the Hazard Ratio (HR) for mortality with accompanying 95% confidence interval (CI) for native Danes compared with other ethnic groups separately. HRs were stepwise adjusted for covariates to study potential mediators of the association of ethnicity with mortality.[12;13] Cox proportional hazards analysis was used to explore whether time living in Denmark before the start of dialysis was associated with mortality on dialysis. For this analysis, only immigrant patients were included. We divided the immigrant group into three a priori defined subgroups based on the number of years living in Denmark before the start of dialysis (≤10 years, >10 to ≤20 years, and >20 years). HRs for mortality with accompanying 95% CIs were calculated for each subgroup, with patients living in Denmark for >20 years as reference group. These HRs were stepwise adjusted for covariates to study underlying mechanisms. Proportional hazards assumptions were tested graphically with cumulative residuals. Covariates had no missing data, except for data on household income (<1% missing). For these missing data we used income closest to the year of interest. Significance levels were determined at p-value ≤0.05. Analyses were carried out with SAS version 9.2, SAS Institute Inc.

Ethical considerations

We obtained permission from the Danish Data Protection Agency and the Danish Society of Nephrology to access individual level patient data.

RESULTS

Baseline characteristics

Within the study period, 9,170 patients aged ≥18 years initiated HD or PD as their first renal replacement therapy in Denmark and continued dialysis treatment for at least 90 days. Of these patients, 46 patients were excluded because they had no data on country of origin and 15 patients were excluded because they originated from 'other regions' (n=8 East Asia, n=1 central America, n=5 South America, n=1 the Caribbean). Of the 9,109 patients eligible for analyses, 633 (7%) were immigrants and 17 (0.2%) descendants. Of all immigrants and descendants, 344 originated from North America, Europe, or Oceania; 79 from North Africa or West Asia; 173 from South or South-East Asia; and 54 from Sub-Saharan Africa. The countries of origin of immigrants and descendants are shown in data supplement 1. Table 1 gives the baseline characteristics of different ethnic groups. Native Danes were older, were less often in the lowest tertile of household income, and had different primary kidney diseases compared with most other ethnic groups.

Follow-up and outcomes

Table 2 gives the follow-up time and incidence rates for different outcomes according to patients' region of origin. The median follow-up time in the total study population was 23.2 months (inter quartile range 9.4-46.0). Crude death rates were highest among native Danes and lowest among patients originating from Sub-Saharan Africa. After age-standardization, native Danes still had higher death rates compared with other ethnic groups, except for patients originating from Sub-Saharan Africa (the latter group had a wide CI). Crude renal transplantation rates were lowest among native Danes and highest among patients originating from Sub-Saharan Africa. After age-standardization, native Danes had similar renal transplantation rates compared with other groups. Among all ethnic groups, no emigrations were documented. No differences were found in cause of death between ethnic groups (data not shown).

Table 1. Baseline characteristics of 9,109 patients who started chronic dialysis treatment in Denmark between 1995 and 2010, according to patients' region of origin.

	Region of origin				
	Denmark (n=8459)	**North America, Europe †, Oceania (n=344)**	**North Africa, West Asia (n=79)**	**South Asian, South-East Asian (n=173)**	**Sub-Saharan Africa (n=54)**
Socio-demographic					
Age *years*	63.2 (14.7)	57.7* (16.1)	52.5* (15.1)	53.8* (15.5)	46.2* (14.0)
Sex *% men*	64	59	63	51*	69
Household income *% lowest tertile* ‡	32	41*	39*	47*	43
Immigrants *%* §	-	96	100	99	100
Clinical					
Number of days admitted to hospital in 30 days after the start of dialysis	3 (0-12)	3 (0-13)	4 (0-13)	2 (0-8)	2 (0-7)
Dialysis modality ‖ *% hemodialysis*	69	69	81*	70	76
Primary kidney disease %					
Diabetes Mellitus	23	27	35*	35*	13
Glomerulonephritis	10	13	19*	16*	26*
Renal vascular disease	12	14	10	9	19
Other	54	46	35*	39*	43
Comorbidity ‡					
Number of days admitted to hospital	7 (2-19)	6 (2-15)	5 (2-14)	9 (2-16)	3.5* (1-10)
Charlson comorbidity index	3 (2-5)	2 (2-5)	2 (2-5)	3 (2-5)	2* (2-3)
Hospital admissions due to cardiovascular disease *%* ¶	5	4	4	4	0
Hospital admissions due to cancer *%*	6	3*	1	1*	2
Medication ‡					
Anti-hypertensive *%*	88	85*	85	83*	67*
Anti-diabetic *%*	24	27	38*	38*	7*

Values are presented as mean (SD) or median (interquartile range) or percentage.

* p-value ≤ 0.05 (compared with patients originating from Denmark).

† Excluding Denmark.

‡ In year prior to the start of dialysis.

§ Versus descendants.

‖ At start of dialysis treatment.

¶ Cardiovascular disease defined as myocardial infarction and/or stroke.

Table 2. Median follow-up time and incidence rates of different outcomes of patients who started chronic dialysis treatment in Denmark between 1995 and 2010, according to patients' region of origin.

	Region of origin									
	Denmark (n=8459)		**North America, Europe *, Oceania (n=344)**		**North Africa, West Asia (n=79)**		**South Asian, South-East Asian (n=173)**		**Sub-Saharan Africa (n=54)**	
Median follow-up *months (IQR)*	22.6	(9.2-45.0)	26.9	(10.6-50.4)	29.4	(15.3-63.4)	28.6	(13.7-54.5)	26.3	(11.1-63.4)
Crude incidence rates *per 1000 py*										
Death	234		166		96		110		53	
Renal transplantation	63		83		85		91		117	
Recovery of renal function	11		3		4		0		0	
Emigration	0		0		0		0		0	
Age-standardized incidence rates *per 1000 py (95% CI)*										
Death	231	(224-237)	195	(165-225)	113	(67-159)	142	(103-182)	239	(0-496)
Renal transplantation	66	(62-69)	61	(48-75)	60	(35-86)	65	(47-84)	87	(40-135)
Recovery of renal function	11	(10-13)	3	(0-6)	2	(0-6)	0		0	
Emigration	0		0		0		0		0	

Abbreviations: IQR = interquartile range; py = person-years; CI = confidence interval.

* Excluding Denmark.

Survival

The cumulative mortality curves during 10 years of follow-up show that native Danes had the highest mortality, followed by respectively patients originating from (2) North America, Europe (excluding Denmark), or Oceania; (3) South Asia or South-East Asia; (4) North Africa or West Asia; and (5) Sub-Saharan Africa (Figure 1). Table 3 shows that native Danes had a greater estimated hazard for mortality compared with all other ethnic groups, both crude and after adjustment for differences in socio-demographic and clinical characteristics. Similar patterns of associations were observed when descendants were excluded from the analyses (data not shown). Stratified analyses for age revealed that the higher mortality for native Danes compared with other ethnic groups was present both among patients ≤50 and >50 years of age (although in some strata 95% CIs were wider and included 1) (data supplement 2).

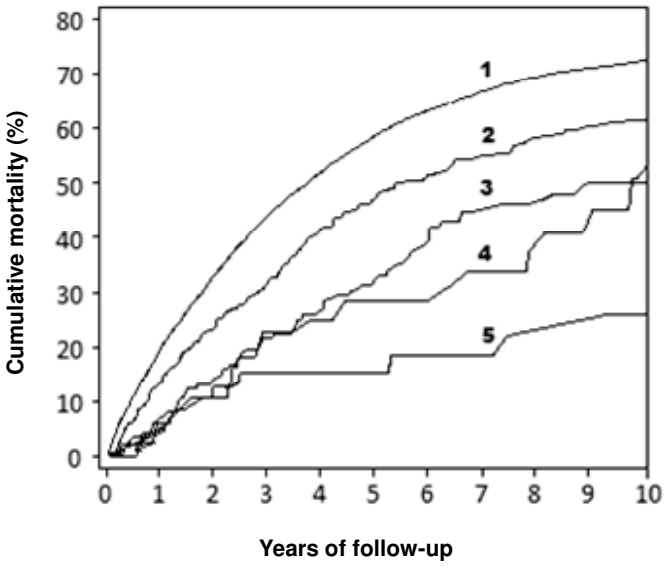

Figure 1. Cumulative mortality curves during 10 years of follow-up for incident dialysis patients in Denmark with different regions of origin, taking account of renal transplantation as competing end point: (1) native Danes; (2) patients originating from North America, Europe (excluding Denmark), or Oceania; (3) patients originating from South Asia or South-East Asia; (4) patients originating from North Africa or West Asia; (5) patients originating from Sub-Saharan Africa.

Table 3. Hazard ratios for mortality for patients originating from Denmark compared with patients originating from other regions, adjusted using more complex multivariable models.

	Region of origin *							
	Denmark *versus* North America, Europe, Oceania		**Denmark *versus* North Africa, West Asian**		**Denmark *versus* South Asia, South-East Asia**		**Denmark *versus* Sub-Saharan Africa**	
Model †	**HR**	**(95% CI)**	**HR**	**(95% CI)**	**HR**	**(95% CI)**	**HR**	**(95% CI)**
1. Unadjusted	1.41	1.22 – 1.63	2.45	1.69 – 3.56	1.97	1.56 – 2.50	4.35	2.40 – 7.87
2. Demographic	1.21	1.04 – 1.40	1.96	1.35 – 2.84	1.59	1.25 – 2.02	2.48	1.37 – 4.48
3. Socioeconomic	1.23	1.06 – 1.43	2.03	1.40 – 2.95	1.64	1.30 – 2.09	3.14	1.45 – 4.74
4. Clinical	1.32	1.14 – 1.54	2.22	1.51 –3.23	1.79	1.41 – 2.27	2.00	1.10 – 3.57

Abbreviations: HR = hazard ratio for mortality; CI = confidence interval.

* Number of patients: Denmark n=8459; North America, Europe, Oceania n=344; North Africa, West Asian n=79; South Asia, South-East Asia n=173; Sub-Saharan Africa n=54.

† Model 1: unadjusted. Model 2: adjusted for age and sex. Model 3: further adjusted for household income. Model 4: further adjusted for dialysis modality, primary kidney disease, number of days admitted to hospital in 30 days after the start of dialysis, number of days admitted to hospital in year prior to start dialysis, Charlson comorbidity index, whether a patient was admitted to hospital due to cardiovascular disease and/or cancer in year prior to start dialysis, use of anti-hypertensive medication and/or anti-diabetic medication.

Duration of residence

Table 4 shows that immigrants living in Denmark for ≤10 years had a lower hazard for mortality compared with those living in Denmark for >20 years. After adjustment for differences in demographic and socioeconomic characteristics, immigrants living in Denmark for ≤10 years still had a lower hazard for mortality compared with those living in Denmark for >20 years. This lower rate for mortality was partly explained by clinical characteristics. Immigrants living in Denmark between 10 and 20 years also had a lower hazard for mortality compared with those living in Denmark for >20 years, but this difference in mortality was less pronounced compared with the differences in mortality between immigrants living in Denmark for ≤10 years and those >20 years. Analyses stratified for Western immigrants (i.e. immigrants originating from North-America, Europe, or Oceania) and non-Western immigrants (i.e. immigrants originating from North Africa, West Asia, South Asia, South-East Asia, or Sub-Saharan Africa) revealed similar patterns of associations, although 95% CIs were wider and included 1 (Table 4).

Table 4. Years living in Denmark before starting dialysis and associated risk of mortality for immigrants who started chronic dialysis treatment in Denmark between 1995 and 2010.

		All immigrants (n = 633)		**Western immigrants * (n =329)**		**Non-Western immigrants † (n =304)**	
Model ‡	**Years living in Denmark §**	**HR**	**(95% CI)**	**HR**	**(95% CI)**	**HR**	**(95% CI)**
1. Unadjusted	≤ 10	0.37	0.26-0.53	0.30	0.18-0.50	0.54	0.33-0.89
	>10 - ≤20	0.57	0.42-0.79	0.64	0.42-0.98	0.60	0.36-0.99
	>20	*Reference*		*Reference*		*Reference*	
2. Demographic	≤ 10	0.59	0.41-0.85	0.56	0.33-0.97	0.64	0.38-1.07
	>10 - ≤20	0.77	0.56-1.06	0.84	0.55-1.28	0.73	0.44-1.26
	>20	*Reference*		*Reference*		*Reference*	
3. Socioeconomic	≤ 10	0.58	0.40-0.84	0.54	0.31-0.95	0.65	0.39-1.10
	>10 - ≤20	0.76	0.55-1.05	0.82	0.54-1.26	0.72	0.43-1.21
	>20	*Reference*		*Reference*		*Reference*	
4. Clinical	≤ 10	0.64	0.44-0.94	0.62	0.35-1.13	0.80	0.45-1.43
	>10 - ≤20	0.71	0.51-0.98	0.81	0.52-1.26	0.76	0.43-1.34
	>20	*Reference*		*Reference*		*Reference*	

Abbreviations: n = number of patients; HR = hazard ratio; CI = confidence interval.

* Immigrants from North America, Europe, and Oceania.

† Immigrants from North Africa, West Asia, South Asia, South-East Asia, and Sub-Saharan Africa.

‡ Model 1: unadjusted. Model 2: adjusted for age and sex. Model 3: further adjusted for household income. Model 4: further adjusted for dialysis modality, primary kidney disease, number of days admitted to hospital in 30 days after the start of dialysis, number of days admitted to hospital in year prior to start dialysis, Charlson comorbidity index, whether a patient was admitted to hospital due to cardiovascular disease and/or cancer in year prior to start dialysis, use of anti-hypertensive medication and/or anti-diabetic medication.

§ Before starting dialysis.

Patient numbers:

≤10 years: all immigrants n=158; Western immigrants n=67; Non-Western immigrants n=91.

>10 ≤20 years: all immigrants n=154; Western immigrants n=70; Non-Western immigrants n=84.

>20 years: all immigrants n=321; Western immigrants n=192; Non-Western immigrants n=129.

DISCUSSION

This large scale epidemiological study involving incident chronic dialysis patients in Denmark, demonstrated that native Danes exhibited a substantially higher mortality rate compared with patients originating from Sub-Saharan Africa, South or South-East Asia, North Africa or West Asia, and North America, Europe (excluding Denmark) or Oceania. Even more interesting, it was shown that the survival advantage for immigrants became smaller with increased duration of residence in Denmark.

To our knowledge, this is the first study showing that the survival of immigrant dialysis patients depends on the duration of residence in the immigration country. In the general population it has been demonstrated that duration of residence is association with mortality [30-32], but to our knowledge not among dialysis patients. Another novel finding of our study is that chronic dialysis patients originating from other Western countries have better survival rates compared with native patients. Furthermore, as far as we know, it has not been demonstrated that immigrant dialysis patients originating from Arabic countries have better survival rates compared with native dialysis patients.

Strengths of our study include the use of an unselected national cohort, the linkage of national registries, and the availability of detailed information on country of birth and duration of residence. There are also some possible limitations. Firstly, although country of birth renders objective information on region of origin, it does not capture the multidimensional character of ethnicity.[33] Ethnicity has been defined as the social group a person belongs to as a result of a mix of cultural and other factors including language, diet, religion, ancestry, and physical features.[34] However, there is no measurable entity of ethnicity that captures all these aspects. Moreover, country of birth is the most frequently used proxy of ethnicity in register-based studies.[24] Secondly, we had limited data on comorbidity. We partly addressed this limitation by using diagnoses of hospital admissions, outpatient contacts and prescribed medications in the year prior to the start of dialysis. In doing so, we may have slightly underestimated comorbidity since patients may have had comorbid diseases without contacting a hospital in the year before starting dialysis. Thirdly, although registered remigrations have been documented among immigrants and descendants, data on unregistered remigration followed by death in the home country were not available. This may have led to an underestimation of the number of deaths in immigrants and descendants. Finally, we did not have information on individual lifestyle

factors, e.g. smoking, drinking, and physical activity. This prevents us from identifying the role of these factors in the differences in survival.

Several explanations for the better survival of immigrants and descendants compared with native Danish patients could be proposed. Before doing so, it should be noted that the better survival of immigrants and descendants compared with native Danish patients is somewhat counterintuitive as immigrants have been documented to have more problems in accessing both primary and secondary care.[35] However, dialysis care is very structured and in accordance with uniform guidelines, which may help prevent inequality in the treatment given.

Firstly, migration factors could possibly explain ethnic differences in survival on dialysis. In the present study, it is demonstrated that patients originating from other Western counties have a better survival compared with native Danes, while both groups are likely to be white. These data suggest that there may be a selection of healthy individuals into migration in the home country.[36] Healthy conditions that are required to migrate may still be present at the start of dialysis and may explain ethnic differences in survival on dialysis. Our finding that the survival advantage for immigrants becomes smaller with increased duration of residence in Denmark may also indicate that migration factors play a role in ethnic differences in survival on dialysis, because healthy conditions that are required to migrate may dissipate over time.

Secondly, environmental factors could possibly explain ethnic differences in survival on dialysis. A Danish survey on health behavior shows that immigrants in Denmark experience healthier lifestyles than native Danes.[37] Furthermore, there are indications that the longer immigrants remain in a Western immigration country, the more deteriorating health they experience, apparently due to the adoption of the lifestyle of the immigration country.[30-32] Unfortunately, in the present study we did not have data on individual lifestyle factors. However, the finding that the survival advantage for immigrants becomes smaller with increased duration of residence in Denmark may suggest that ethnic differences in survival on dialysis are (at least partly) due to protective health practices of immigrants.

Thirdly, genetic variability may account for ethnic differences in survival on dialysis. Nonetheless, to be an explanation for ethnic differences in survival genes should operate through intermediating clinical parameters. Many clinical parameters presently known to influence mortality have been previously adjusted for in multivariable models.[2-13] With the

exception of one study in which the effect of race/ethnicity on survival was no longer significant after case-mix adjustment[9], in most studies clinical parameters did not appear to explain ethnic differences in survival on dialysis.[2-13] However, most models assumed that the effect of a covariate on mortality is equal among ethnic groups (no or limited effect modification tested) and that there is no interaction between different factors (models did not include interaction terms), whereas growing evidence suggests that these are incorrect assumptions.[8;38-40] In the present study, we were not able to test effect modification due to sample size limitations.

Finally, differences in the trajectory prior to the start of dialysis between ethnic groups can introduce substantial selection bias. For example, it has been demonstrated that mortality among blacks with chronic kidney disease (CKD) in the predialysis period is higher than predialysis mortality among whites with CKD, which may result in the selection of relatively healthier black patients who ultimately require dialysis.[41]

CONCLUSION

We demonstrated ethnic differences in survival on dialysis in Denmark that were beneficiary to immigrants and their descendants. A challenging new finding is that the survival advantage for immigrants became smaller with increased duration of residence in Denmark. Future studies should focus on the relative importance of migration factors, environmental factors, and genetic factors as explanations for ethnic differences in survival on dialysis and should focus on effect modification and interaction. These studies may offer important insights that could be used as starting points for research improving the survival of dialysis patients.

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Supplementary Table 1. Country of origin of 650 study patients.

North America, Europe, Oceania (n=344)	**North Africa, West Asia (n=79)**	**South Asia, South-East Asia (n=173)**	**Sub-Saharan Africa (n=54)**
North America	**North Africa**	**South Asia**	**Sub-Saharan Africa**
8 USA	15 Morocco	61 Pakistan	25 Somalia
3 Canada	5 Egypt	29 Sri Lanka	4 Kenya
	2 Algeria	16 Iran	4 Nigeria
Europe		11 India	3 Congo
273 EU	**West Asia**	6 Afghanistan	3 Ghana
46 Bosnia	21 Lebanon	2 Bhutan	2 Eritrea
3 Yugoslav	19 Iraq	1 Bangladesh	2 Ethiopia
2 Croatia	4 Jordan		2 Sierra Leone
2 Russia	3 Israel	**South-East Asia**	2 Tanzania
1 Kosovo	2 Syrian	19 Vietnam	2 Uganda
1 Ukraine	1 Armenia	12 Philippines	1 Benin
	1 Azerbaijan	9 Thailand	1 Botswana
Oceania	1 Palestinian Territory	3 Indonesia	1 Burundi
2 Australia	*5 Middle East* *	1 Malaysia	1 Mozambique
1 New Zealand		1 Myanmar	1 South Africa
2 Oceania[1]		1 Singapore	
		1 Asia[1]	

633 patients were immigrants and 17 patients were descendants (descendants originated from EU (n=13), Canada (n=1), Australia (n=1), Iran (n=1), and Pakistan (n=1).

* not further specified.

Supplementary Table 2. Hazard ratios for mortality for patients originating from Denmark compared with patients originating from other regions stratified for patients ≤ 50 and >50 years of age and adjusted using more complex multivariable models.

	Region of origin							
	Denmark † *versus* North America, Europe, Oceania ‡		**Denmark † *versus* North Africa, West Asian §**		**Denmark † *versus* South Asia, South-East Asia ‖**		**Denmark † *versus* Sub-Saharan Africa ¶**	
Model *	**HR**	**(95% CI)**	**HR**	**(95% CI)**	**HR**	**(95% CI)**	**HR**	**(95% CI)**
≤ 50 YEARS								
1. Unadjusted	2.02	1.28-3.18	3.72	1.09-10.52	2.04	1.12-3.72	5.46	1.75-16.95
2. Demographic	1.78	1.13-2.82	3.09	0.99-9.62	2.02	1.11-3.68	4.44	1.43-13.89
3. Socioeconomic	1.82	1.15-2.89	2.95	0.95-9.17	2.05	1.13-3.73	4.63	1.48-14.49
4. Clinical	1.67	1.05-2.65	2.51	0.80-7.87	1.81	0.98-3.32	3.17	1.01-9.90
> 50 YEARS								
1. Unadjusted	1.24	1.06-1.45	2.16	1.46-3.21	1.74	1.35-2.26	2.01	1.00-4.02
2. Demographic	1.14	0.98-1.33	1.84	1.24-2.72	1.51	1.17-1.96	1.70	0.85-3.40
3. Socioeconomic	1.16	1.00-1.36	1.94	1.31-2.88	1.59	1.23-2.06	1.78	0.89-3.57
4. Clinical	1.27	1.09-1.49	2.19	1.47-3.25	1.80	1.39-2.34	1.41	0.70-2.82

Abbreviations: HR = hazard ratio for mortality; CI = confidence interval.

* Model 1: unadjusted. Model 2: adjusted for age and sex. Model 3: further adjusted for household income. Model 4: further adjusted for dialysis modality, primary kidney disease, number of days admitted to hospital in 30 days after the start of dialysis, number of days admitted to hospital in year prior to start dialysis, Charlson comorbidity index, whether a patient was admitted to hospital due to cardiovascular disease and/or cancer in year prior to start dialysis, use of anti-hypertensive medication and/or anti-diabetic medication.

† ≤ 50 years: n=1569; > 50 years n= 6890.

‡ ≤ 50 years: n=99; > 50 years n= 245 (Europe = excluding Denmark).

§ ≤ 50 years: n= 30; > 50 years n= 49.

‖ ≤ 50 years: n= 68; > 50 years n=105.

¶ ≤ 50 years: n=33; > 50 years n= 21.

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