Ethnic differences in survival on dialysis in Europe
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General discussion
The general objective of this thesis was to investigate to what extent and why ethnic differences in survival on dialysis exist in European countries. In this chapter, an overview of the main findings is given and methodological issues of the studies presented in this thesis are considered. Furthermore, explanations for ethnic differences in survival on dialysis are discussed and clinical implications, recommendations for future research and main conclusions are provided.

**MAIN FINDINGS**

In the North-American subcontinent, non-white dialysis patients have a better survival than white dialysis patients. Although extensively studied, these findings are not completely understood. It was postulated that exploring ethnic survival disparities on dialysis in Europe may help to identify factors responsible for ethnic differences in survival on dialysis (chapter 1).

By reviewing the literature, it was shown that a limited number of studies on non-white dialysis patients in Europe are available. Consequently, it was concluded that there is a need for carefully and systematically collected data on the survival of non-white dialysis patients in Europe (chapter 2).

Firstly, survival data were analyzed from native and immigrant dialysis patients who entered a renal service of an urban hospital in the Netherlands. Increased survival in immigrant compared with native dialysis patients was demonstrated and it was shown that this survival advantage is only partly explained by a younger age of immigrants at the start of dialysis (chapter 3).

Subsequently, ethnic differences in survival on dialysis were studied in a multicenter setting in the Netherlands with emphasis on whether psychosocial factors explain ethnic survival differences (chapter 6). The following psychosocial factors were studied: health related quality of life (HRQoL), depressive symptoms, self-rated health, marital status, education level, employment status and having children. To measure depressive symptoms, an instrument was used of which we had demonstrated that it has high discriminatory capacities in screening for depressive symptoms in dialysis patients (chapter 4). A long follow-up period was used since we had demonstrated that the presence of depressive
symptoms in the initial period of dialysis treatment is an independent risk factor for mortality in the short-, medium- and long-term (chapter 5). It was concluded that white dialysis patients have a three-fold higher mortality risk compared with black patients, but an equal mortality risk compared with Asian patients (chapter 6). No evidence was found for psychosocial factors being an explanation for ethnic differences in survival on dialysis.

Due to sample size limitations, in chapter 3 and 6 we were not able to study whether the effects of covariates on mortality differ between ethnic groups (i.e. to study effect modification). Therefore, an analysis was performed in a much larger series of patients from the United Kingdom Renal Registry (UKRR). In chapter 7, we studied whether the association of mineral metabolism disorders with mortality is equal among white, black and South Asian patients initiating dialysis treatment. In this chapter, white patients were shown to be more likely to die on dialysis than black and South Asian patients. Ethnic differences were demonstrated in the association of calcium, phosphate and PTH levels with mortality.

Next, ethnic differences in survival among incident dialysis patients in Denmark were studied. Native Danes were shown to have a greater estimated hazard for mortality compared with patients originating from other regions in the world. Even more interestingly, it was demonstrated that the survival advantage for immigrants became smaller with increased duration of residence in Denmark (chapter 8).

Finally, we studied whether black and white patients starting pre-dialysis care in the Netherlands have differences in the time until the start of renal replacement therapy and in rate of decline in renal function. It was shown that blacks have a faster renal function decline than whites in the period leading up to the start of dialysis (chapter 9).

**Methodological issues**

Before discussing explanations for ethnic differences in survival on dialysis, the internal and external validity of the studies presented in this thesis will be discussed. Specific methodological issues of the studies that are included in this thesis have been discussed in the individual chapters.
Internal validity

Internal validity refers to the validity of the inferences for the source population of the study subjects. Internal validity can be affected by two types of error: random error and systematic error.\(^1\)

Firstly, internal validity can be affected by random error. An important source of random error is the lack of precision of the estimates. Precision of the estimates is reflected by the width of the confidence interval around the point estimate.\(^2\) This source of random error can be minimized by increasing the sample size. In most studies described in this thesis, relatively large patient groups have been included and therefore confidence intervals around the point estimates were rather small. However, in most studies, the number of minority patients was still quite small. This limited the possibilities to perform subgroup analyses. In chapter 7, using data of the comprehensive UKRR, we were able to study subgroups. Nonetheless, after dividing patients into subgroups based on ethnicity and calcium, phosphate and PTH levels, some subgroups were still relatively small and consequently confidence intervals around the point estimates were relatively wide.

Another source of random error is random or nondifferential misclassification.\(^3\) This misclassification can occur in both exposure and outcome, and is difficult to avoid completely in large scale epidemiological and registry based studies. Nondifferential misclassification generally results in an underestimation of real effects. However, there is no reason to believe this problem occurred more in our studies than in any other observational study published.

Secondly, internal validity can be affected by systematic error. Systematic error reflects a problem of validity of the study.\(^3\) Systematic error is referred to as bias and leads to conclusions that systematically underestimate or overestimate the true relationship between the exposure and the outcome. In general, three broad categories of bias can be identified: selection bias, information bias and confounding.\(^1\) Whether these forms of bias have threatened the interval validity of the results is discussed below.

Selection bias

Selection bias arises when the relation between the exposure and the outcome is different for those who participate from those who do not participate but should be theoretically
eligible for study.\textsuperscript{3} At least three forms of selection bias might have threatened the internal validity of our results. These forms are discussed below.

The first form of selection bias is related to the ability to speak the domestic language. In the NECOSAD cohort (chapter 5 and 6) and in the PREPARE-II cohort (chapter 9), only patients who understood the Dutch language were included. This might have resulted in the selection of patients who are relatively well integrated in the Dutch society. If the degree of integration is associated with the outcome, these studies might be subject to selection bias. In chapter 8, we found indications that degree of integration could indeed be associated with outcome. We demonstrated that an increased duration of residence in the host country is associated with an increased mortality. Hence, the ethnic differences in survival demonstrated in chapter 6 may be an underestimation of the real effect.

The second form of selection bias is related to informative censoring. In chapter 3, the Kaplan-Meier analysis was used to calculate survival curves of native and immigrant dialysis patients. An important assumption of the Kaplan-Meier method is that censoring is independent of the event of interest (so called non-informative censoring).\textsuperscript{4} In the Kaplan-Meier analysis in chapter 3 renal transplantation was treated as a censored event, whereas the probability of getting a renal transplantation is related to the mortality risk (patients who receive a renal transplant are usually healthier than patients who do not).\textsuperscript{5} Therefore, survival curves in chapter 3 may be an underestimation of the real survival. For this reason, in chapter 6 and 8 we chose to use competing risk analysis to calculate cumulative mortality curves. Renal transplantation was taken into account as a competing end-point.

The third form of selection bias is related to missing data. In chapters 3-9, we encountered the problem of missing data. Missing data could lead to biased results. Whether this occurs depends on the amount of missing data, the type of missing data and the technique used to handle these data. To explain briefly, in general three types of missing data can be identified: missing completely at random (MCAR), missing at random (MAR), and missing not at random (MNAR). When missing data are MCAR, the probability of missingness does not depend on observed or unobserved data. Individuals with missing data that are MCAR are a random subset of the total study population. When missing data are MAR, the probability of missingness depends on other, observed, patient characteristics. Missing data that are MAR can be predicted based on other, observed, patient characteristics. When missing data are MNAR, the probability that an observation is missing depends on unobserved patient
characteristics. Systematic differences exist between the patients with missing data who are MNAR and patients without missing data.  

We used various techniques to handle missing data. In chapters 3 and 4, missing values were substituted by the mean of the known values. However, this method could result in biased estimates. For example, in chapter 4 this method might have resulted in an underestimation of the presence of depressive symptoms among the study patients, since it is likely that patients who are suffering from depressive symptoms have a higher probability of not completing items in self-report questionnaires on depressive symptoms (MAR or MNAR). However, we consider it unlikely that results in chapters 3 and 4 are profoundly biased, since the amount of missing data was very low. In chapters 5, 6, 7 and 9, we used a more sophisticated method of handling missing data: multiple imputation. In these chapters, missing data were imputed by a value that is predicted using the patient’s available characteristics under the assumption of MAR (we assumed that missing data were MAR after comparing characteristics of patients with and without missing data). Multiple imputation results in unbiased estimates of study associations and correctly estimated standard errors and confidence intervals.  

In chapter 8, covariates had no missing data except for income (<1% missing, replaced by the income closest to the year of interest).

**Information bias**

Information bias arises when the information collected from or about study subjects leads to results that are consistently either too large or too small. At least three forms of information bias might have threatened the internal validity of our results. These forms are discussed below.

The first form of information bias is related to the classification of ethnicity. In the chapters in which ethnic groups were classified using perceived ethnicity by medical staff (chapters 5, 6, 9), the degree of patients’ integration may have influenced the classification. If a patient was highly integrated in the Dutch society, a healthcare worker may have classified this patient as white, while he or she was non-white. Furthermore, different approaches to classify ethnicity may have resulted in different classifications. This is further discussed in a separate section below (paragraph ‘concept of ethnicity’).

The second form of information bias is related to interpretation of questionnaires. In chapter 4-6, we used data that were based on self-report questionnaires. Patients of different ethnic
origins may have responded differently to questionnaires, for example because of differences in interpretation of items or differences in tendency to give socially desirable answers. If these responses do not reflect differences in patients’ behavior, this may have led to cultural bias.

The third form of information bias is related to the use of registry data. In chapter 8, we used data obtained from national registries. Data on comorbidities, prescribed medication and income were based on patient data from the year prior to the start of dialysis. Consequently, patients who migrated to Denmark in the year prior to the start of dialysis, may have been incorrectly classified as having no comorbidity, no prescribed medication or a low income.

**Confounding**
Confounding occurs when the effect of the determinant on the outcome is mixed with the effect of another variable. In general, there are three criteria for a variable to be regarded as a confounding factor: (1) the variable must be a risk factor for the outcome, (2) the variable must be associated with the determinant in the study population, and (3) the variable must not be an intermediate step in the causal path between the determinant and the outcome. Whether confounding play a role in the studies described in this thesis is discussed below.

In the studies described in chapters 3, 6, 8 and 9, we explored the association between ethnic origin and an outcome (in chapters 3, 6 and 8 the outcome was death; and in chapter 9 the outcome was the start of renal replacement therapy). In general, ethnic origin can be regarded as a factor that precedes all other factors in life. Consequently, all other variables that are associated with ethnic origin and with the outcome are intermediate steps in the causal path between ethnic origin and the outcome. Therefore, we argued that in the studies described in chapters 3, 6, 8 and 9, there are no confounding effects.

In most epidemiological studies, multivariate adjustment is done to get rid of confounding effects. In chapter 3, 6, 8 and 9, we used multivariate adjustment despite arguing that in these studies there were no confounding effects. In these studies, multivariate adjustment was applied to explore mechanisms underlying the association between ethnicity and the outcome. In other words, we adjusted for intermediates in the causal path between the determinant and the outcome to explore mechanisms underlying the association between
ethnicity and the outcome. Thus, although we applied multivariate adjustment in chapters 3, 6, 8 and 9, we did not adjust for confounding effects.

The study described in chapter 7 is a special example of this. The aim of this study was to explore the effect of ethnic origin on ‘the effect of disordered mineral metabolism on mortality’. The variables we adjusted for were intermediates in the causal path between the determinant (ethnic origin) and the outcome (the effect of disordered mineral metabolism on mortality). Again, adjustments were made to explore whether the effects were independent of the variables we adjusted for, instead of to get rid of confounding effects.

In chapter 5, we were not primarily interested in ethnicity. In this chapter we studied the association between the presence of depressive symptoms and mortality over time. In this study, there were potential confounding effects. For example, the presence of comorbidity could be a confounding factor. To get rid of these possible confounding effects, we adjusted for differences in several patient characteristics. However, as in all epidemiological studies, residual confounding may still have been present.

**External validity**

External validity refers to the generalizability of the study results. In line with studies from the North-American subcontinent, we demonstrated better survival for ethnic minority patients compared with majority patients on dialysis in Europe (except for an equal survival for Asian compared with white dialysis patients in the Netherlands). Because of this rather consistent finding, we suppose that the better survival for ethnic minority patients is generalizable to most ethnic minority groups on dialysis in Europe.

Whether our study results are generalizable to other continents than Europe and North-America is currently unknown. Scant data are available on the survival of ethnic minority groups on dialysis in other continents. These data, however, are highly important as they provide further insight into the mechanisms underlying ethnic differences in survival on dialysis. For example, these data give insight in whether ethnic survival differences are related to the ethnic minority status of dialysis patients or to differences in genotypes (in some continents white patients belong to an ethnic minority group).

Recently, a small number of studies related to the survival of ethnic minority patients on dialysis in other continents have been published. Chronic dialysis patients in Israel who are
ethnically Arab exhibited better survival than Jewish Israelis. In Australia and New Zealand, it was found that indigenous dialysis patients had higher mortality rates than non-indigenous patients. Furthermore, the results of another study we have worked on show that ethnic minority groups on peritoneal dialysis in Brazil have better survival compared with white patients.

EXPLANATIONS FOR ETHNIC DIFFERENCES IN SURVIVAL ON DIALYSIS

In this section, the concept of ethnicity will be considered and a theoretical framework illustrating possible pathways underlying ethnic differences in survival on dialysis will be presented. Next, explanations for ethnic differences in survival on dialysis are discussed.

Concept of ethnicity
Ethnicity is a difficult concept. We used the following definition for ethnicity, provided by Bhopal: ‘Ethnicity is the social group a person belongs to, and either identifies with or is identified with by others, as a result of a mix of cultural and other factors including one or more of language, diet, religion, ancestry and physical features traditionally associated with race’. Race is defined as ‘the group a person belongs to as a result of a mix of physical features such as skin color and hair texture, which reflect ancestry and geographical origins’. Based on these definitions, we consider ethnicity as a multidimensional concept.

In epidemiological studies, different measures have been used to classify ethnicity, such as skin color, country of birth, name analysis and self-assessed ethnic group. Each of these measures is based on a different dimension of ethnicity. Table 1 gives an overview of the measures that have been used in this thesis to classify ethnicity. This table shows that the measures used in this thesis predominantly refer to country of birth and physical features.
Table 1. Overview of the measures that have been used to classify ethnicity and the ethnic groups that have been identified.

<table>
<thead>
<tr>
<th>Chapter</th>
<th>Cohort</th>
<th>Ethnic groups based on</th>
<th>Ethnic groups</th>
<th>Definition of ethnic group</th>
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</thead>
<tbody>
<tr>
<td>3,4</td>
<td>SLAZ</td>
<td>Patients’ country of birth</td>
<td>Native Dutch</td>
<td>Native Dutch: individuals born in the Netherlands Immigrants: individuals born outside the Netherlands</td>
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<tr>
<td></td>
<td>(&amp;VUMC)</td>
<td></td>
<td>Immigrants</td>
<td></td>
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<td>5,6</td>
<td>NECOSAD</td>
<td>Perceived ethnicity by medical staff</td>
<td>Whites</td>
<td>Whites: individuals originating from European countries, Turkey and Morocco Blacks: individuals originating from Sub-Saharan Africa (=including Surinamese Creoles) Asians: individuals originating from Asian countries (=including Surinamese Hindustani)</td>
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<td></td>
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<td>Blacks</td>
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<td>Asians</td>
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<tr>
<td>7</td>
<td>UKRR</td>
<td>Self-reported ethnicity or renal unit ascription</td>
<td>Whites</td>
<td>Whites: individuals originating from European countries Blacks: black Caribbeans, black Africans, black other and black mixed South Asians: individuals originating from India, Pakistan, Bangladesh, other countries of the Indian subcontinent, East African Asians and Asians other non-mixed</td>
</tr>
<tr>
<td></td>
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<td></td>
<td>Blacks</td>
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<td></td>
<td>South Asians</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>DNR</td>
<td>Patients’ country of birth and parents’ country of birth</td>
<td>Native Danes</td>
<td>Native Danes: individuals having at least one parent born in Denmark Immigrants and descendants from: North America, Europe, Oceania North Africa, West Asia South Asia, South-East Asia Sub-Saharan Africa</td>
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<td></td>
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<td>Immigrants</td>
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<td>Descendants</td>
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<tr>
<td>9</td>
<td>PREPARE</td>
<td>Perceived ethnicity by medical staff</td>
<td>Whites</td>
<td>Whites: individuals originating from European countries, Turkey and Morocco Blacks: individuals originating from Sub-Saharan Africa (=including Surinamese Creoles)</td>
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<td>Blacks</td>
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</tbody>
</table>

Abbreviations: SLAZ: Sint Lucas Andreas Hospital, VUMC: VU University Medical Center, NECOSAD: Netherlands Co-operative Study on the Adequacy of Dialysis, DNR: Danish Nephrology Registry, UKRR: United Kingdom Renal Registry, PREPARE: PREdialysis PAtient REcord study.
Theoretical framework
Before discussing explanations for ethnic differences in survival on dialysis, it is important to focus on possible pathways underlying ethnic differences in survival on dialysis. A number of theoretical models have been published illustrating how the association between ethnicity and health appears.\textsuperscript{13} One of these models is the widely used model of Stronks et al.\textsuperscript{14}, showing characteristics of ethnic groups that play a role in the interpretation of ethnic differences in health. Inspired by this model and by extensions of this model\textsuperscript{15,16}, we have created a theoretical framework that illustrates possible pathways underlying the association between ethnicity and survival on dialysis (Figure 1).

\textbf{Figure 1.} Schematic overview of pathways underlying the association between ethnicity and survival on dialysis (inspired by\textsuperscript{14-16}).

This figure is based on the assumption that pathways underlying ethnic differences in survival on dialysis work through explanatory mechanisms. These explanatory mechanisms include genetic factors, cultural factors, factors related to the position in the (host) country and migration factors. Examples of cultural factors are traditions and religion. Examples of factors related to the position in the (host) country are socioeconomic position and residence status. Examples of migration factors are migration history and selection process before migration.
Subsequently, the pathways either directly influence the outcome through health related factors, or work through specific environmental factors, then through health related factors and finally influence the outcome. Specific environmental factors include factors related to lifestyle (e.g. smoking, alcohol use, physical activity, nutrition), healthcare services (e.g. access to healthcare, use of healthcare services, provided treatment), physical environment (e.g. sunlight exposure, toxin exposure), social environment (e.g. social support) and/or psychological stress (e.g. stress related to the migration process).

**Explanations for ethnic differences in survival on dialysis**

In this thesis, we investigated the role of a large number of demographic, clinical and psychosocial factors in ethnic differences in survival on dialysis. The role of these factors and the role of underlying factors (i.e. factors that influence demographic, clinical and psychosocial factors) are discussed below.

**Demographic factors**

We demonstrated that ethnic minority patients were younger at the start of dialysis treatment compared with majority patients. In Amsterdam, immigrant dialysis patients were, on average, 13 years younger compared with native Dutch patients (chapter 3). In the Dutch multicenter study, we found that black and Asian patients were on average 11 and 4 years younger compared with whites, respectively (chapter 6). In the UK, black and South Asian patients were respectively 8 and 6 years younger than whites (chapter 7). In Denmark, compared with native Danes, patients originating from North America, Europe and Oceania were 6 years younger, patients originating from North Africa and West Asia were 11 years younger, patients originating from South Asia and South-East Asia were 9 years younger and patients originating from Sub-Saharan Africa were on average 17 years younger (chapter 8). We demonstrated that the higher mortality risk for native/white dialysis patients attenuated after adjustment for differences in age. This indicates that the better survival for ethnic minority patients is partly explained by differences in age at the start of dialysis treatment (chapter 3, 6, 8).

It is not completely understood why ethnic minority patients were younger at the start of dialysis. A possible explanation is that ethnic minority patients arrive at the final stage of CKD earlier because of a faster decline in renal function. In chapter 9, we demonstrated that blacks indeed have a faster decline in renal function compared with whites in the stage prior to the start of dialysis. In the North American subcontinent, ethnic differences in renal
function decline have also been demonstrated (both in patients with and without CKD\textsuperscript{17,18}). Another possibility is that age differences are, to some extent, a reflection of the age structure in the general population. European studies in the general population have demonstrated a lower mean age among immigrants compared with natives.\textsuperscript{19}

After adjustment for differences in age at the start of dialysis between ethnic groups, ethnic minority patients remained to have a better survival compared with native/white patients. Therefore, other factors do also play a role.

**Clinical factors**

We explored the role of a large number of clinical factors at the start of dialysis, such as body mass index, blood pressure, renal function, primary cause of renal failure, the presence of comorbidities, laboratory measurements, and dialysis adequacy characteristics. After adjustment for differences in these factors in multivariable regression models, we did not find indications that these clinical parameters explain ethnic differences in survival on dialysis (chapter 3, 6, 8). However, this does not imply that clinical factors are not responsible for ethnic differences in survival on dialysis.

Other clinical factors may explain ethnic differences in survival on dialysis, such as differences in prescribed medication between ethnic groups. In a study from the US, it was demonstrated that therapy with activated vitamin D is a potential explanation for ethnic survival disparities on dialysis. Survival advantages of black dialysis patients appeared restricted to those receiving activated vitamin D and the survival advantage for black dialysis patients was lost after adjustment for vitamin D dosage.\textsuperscript{20} In addition, ethnic differences in morbidity during the course of dialysis may explain ethnic differences in survival. These topics should be studied in future research.

Furthermore, in our multivariable regression models, we assumed that the effect of a covariate on mortality is equal among ethnic groups. However, there is growing evidence that this is an incorrect assumption. In chapter 7, we found indications that the association of mineral metabolism disorders with mortality in dialysis patients differs among ethnic groups. In other studies, it has also been found that the effect of covariates on mortality could differ among ethnic groups.\textsuperscript{21,22}
Psychosocial factors

It has been demonstrated that psychosocial factors, such as HRQoL, social support and self-rated health, are independently associated with mortality in chronic dialysis patients. In chapter 5, we demonstrated that the presence of depressive symptoms at the start of dialysis treatment is associated with increased mortality on dialysis. In the literature, favorable psychological conditions have been reported in ethnic minority patients compared with majority patients on dialysis, such as better HRQoL in black compared with white dialysis patients and less depressive symptoms in non-white compared with white dialysis patients. Therefore, in chapter 6 we hypothesized that psychosocial factors explain ethnic differences in survival on dialysis. In this chapter, we studied a large number of psychosocial factors, including HRQoL, depressive symptoms, self-rated health, marital status, education level, employment status and having children. We did not find indications that these factors play a role in ethnic differences in survival on dialysis. However, some important psychosocial factors were not addressed. For example, the role of spirituality and religiosity to cope with end-stage renal disease was not studied. Furthermore, we only investigated psychosocial factors at the start of dialysis treatment, while differences in psychosocial factors between ethnic groups may become more apparent during the course of dialysis treatment. These topics should be investigated in future research.

Underlying factors

As illustrated in Figure 1, demographic, clinical and psychosocial factors are influenced by numerous underlying factors. These underlying factors could be grouped into genetic factors, environmental factors (i.e. specific environmental factors) and migration factors. In literature, the role of these underlying factors in ethnic differences in survival on dialysis has not yet been investigated. In chapter 8, however, important findings were obtained which gave an insight in the relative importance of these factors. Within the group of patients starting dialysis treatment in Denmark, patients originating from other Western countries were found to have better survival rates compared with native Danes. In addition, it was demonstrated that the survival advantage for immigrants becomes smaller with increased duration of residence in Denmark.

These findings provide preliminary evidence that environmental and migration factors play a role in ethnic differences in survival on dialysis. Environmental factors may play a role because duration of residence was associated with mortality risk. The longer immigrants had lived in Denmark, the more their survival pattern resembled the survival of native Danes.
Migration factors may play a role because patients originating from other Western countries had a better survival compared with native Danes, while both groups are likely to be white. It is thus possible that people who migrate from their home country are healthier than average. Our finding that the survival advantage for immigrants became 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.

**IMPLICATIONS AND RECOMMENDATIONS**

In this section, clinical implications of our findings and recommendations for future research will be discussed.

**Clinical implications**

It is important to gain an insight into the underlying reasons for ethnic differences in survival on dialysis as this could provide new ideas or have implications for improved renal replacement therapy for specific ethnic groups. For example, the study presented in chapter 7 could be the starting point for other studies elucidating whether ethnic specific targets in the control of mineral metabolism in dialysis patients are needed. Furthermore, the study presented in chapter 9 leads to the recommendation that black patients with chronic kidney disease should be referred to pre-dialysis care earlier than white patients to assure timely preparation for renal replacement therapy. However, much more attention should be paid to ethnic differences in survival on dialysis and many more studies are needed before we can fully understand survival differences and appreciate clinical implications.

**Recommendations for future research**

As discussed in this chapter, future research should aim at investigating:

- Whether the effects of clinical factors on mortality differ between ethnic groups (effect modification).
- The cross-cultural validity of questionnaires used among dialysis patients.
- The role of morbidity and medication use during the course of dialysis treatment in ethnic differences in survival on dialysis.
- The role of spirituality and religiosity in ethnic differences in survival on dialysis.
• The role of genetic, environmental and migration factors in ethnic differences in survival on dialysis.
• Whether differences in the trajectories prior to the start of dialysis contribute to ethnic differences in survival on dialysis.
• Ethnic differences in survival on dialysis in countries where white patients belong to ethnic minority groups.

**Main Conclusion**

When all our studies are combined, we demonstrated better survival for most ethnic minority groups on dialysis in Europe compared with ethnic majority groups. We found that the better survival for most ethnic minority groups is partly explained by the younger age of ethnic minority patients. We did not find indications that clinical or psychosocial factors explain these differences in survival. Preliminary evidence was provided that environmental and migration factors play a role in ethnic differences in survival on dialysis. The role of these factors and the exact role of clinical and psychosocial factors need to be investigated in future studies.
REFERENCES

10. Fernandes N, Hoekstra T, van den Beukel TO, Tirapani L, Bastos K, Pecoits-Filho R, Qureshi AR, Dekker FW, Bastos MG, Divino-Filho JC: The impact of ethnicity on survival in Brazilian incident peritoneal dialysis patients, accepted for publication in Am J Kidney Dis, 2013


