English Summary
ENGLISH SUMMARY

This thesis is about depressive and anxiety symptoms in chronic dialysis patients and other patients, and is divided in two parts. Part A focused on differences in the prevalence of depressive and anxiety symptoms in native and immigrant (chronic dialysis) patients and various factors (patient characteristics and cultural factors) associated with these symptoms. Part B focused on the association of inflammation and depressive symptoms in chronic dialysis patients.

In chapter 1, an introduction to the research conducted in this thesis was provided. Depressive and anxiety symptoms are highly prevalent in medically ill patients and chronic dialysis patients, and associated with higher morbidity and mortality. Due to immigration the number of non-native citizens in the Netherlands increases and therefore, clinicians will be more often confronted with immigrant patients. In the general population it has been found that the prevalence of depressive and anxiety symptoms is higher in immigrant compared to native patients. It is not clear whether immigrant status is a risk factor for depressive and anxiety symptoms in medically ill or chronic dialysis patients. Acculturation (adaptation to a new cultural context) and negative religious coping might be risk factors for the development of depressive and anxiety symptoms in immigrant chronic dialysis patients.

Furthermore, chronic dialysis patients are known for a chronic inflammatory state. Cross-sectional associations between inflammatory markers and depressive symptoms have been found. However, the direction of this association is unknown and also the mechanism linking inflammatory markers and depressive symptoms is not clear. Finally, longitudinal associations between inflammatory markers and depressive symptoms have not been examined yet.

In chapter 2, the prevalence of psychological distress (i.e. depressive and anxiety symptoms) in a general teaching hospital in Amsterdam was examined, comparing native and immigrant patients. Nine-hundred-four patients were included from October 2011 to January 2012. A high overall prevalence of psychological distress of 58% was found. Compared with native patients (n=585), immigrant patients (n=319) were 1.7 times more likely to have psychological distress. The prevalence was highest in Turkish and Moroccan patients, with prevalences of respectively 79% and 73%. When comparing first and second generation immigrant patients, first generation immigrants were 2.1 times more likely to have psychological distress. We explored whether patient characteristics (socio-demographics, socio-economic status, quality of life, history of psychiatric disease and health care use) could explain these different prevalences between native and immigrant patients and first and second generation immigrant patients. After adjustment for these variables the odds ratios stayed the same. These patient characteristics did not explain the higher prevalence of psychological distress for immigrant and first generation immigrant patients.
Subsequently, we examined in chapter 3 the prevalence of depressive and anxiety symptoms in native and immigrant chronic dialysis patients. Data from the DIVERS study were used, an observational, prospective cohort study among chronic dialysis patients in four large teaching hospitals and one university hospital in the Netherlands. Four-hundred-ninety-four patients were included in the study, 245 native patients and 249 immigrant patients. The prevalence of depressive and anxiety symptoms is respectively 1.8 and 1.7 times higher in immigrant compared to native chronic dialysis patients. The difference in prevalences was highest in Asian patients versus native patients. Again, adjustment for patient characteristics (socio-demographic and clinical factors, comorbidities, laboratory makers and physical status) was performed. Patient characteristics did not appear to explain the higher prevalence of depressive and anxiety symptoms in immigrant chronic dialysis patients. It is possible that an explanation for the higher prevalence may be found in the migration process.

In chapter 4, we examined the association of acculturation and depressive and anxiety symptoms in 249 immigrant chronic dialysis patients included in the DIVERS study. Acculturation is the adaptation of immigrants to a new cultural context and involves both contact and participation in the new society and maintenance of culture and traditions. The questionnaire developed for the Dutch setting measures acculturation on 5 subscales ("Skills", "Social integration", "Traditions", "Values and norms" and "Loss"). Less skills for living in the new society and feelings of loss were associated with more depressive and anxiety symptoms in immigrant chronic dialysis patients. However, we did not find the expected protective effect of maintenance of culture and traditions ("Traditions" and "Values and norms"). Therefore, the higher prevalence of depressive and anxiety symptoms in immigrant patients is at least partly explained by less skills and feelings of loss.

In chapter 5, the association between religious behavior, positive and negative religious coping and depressive and anxiety symptoms is assessed in both native and immigrant chronic dialysis patients. It has been found that negative religious coping (religious struggle) is associated with more psychological distress in chronic dialysis patients. Secularization in the Netherlands progresses, while immigrants are more often religious. Therefore, we proposed that religious struggle could also explain the higher prevalence of depressive and anxiety symptoms in immigrant chronic dialysis patients. Two-hundred-sixty native and 261 immigrant patients were included from the DIVERS study. We found no significant associations between religious behavior and depressive and anxiety symptoms in both groups. Strong significant associations were found for negative religious coping items with depressive and anxiety symptoms in native and immigrant patients. Similar impact of negative religious coping on depressive and anxiety symptoms was found for both native and immigrant chronic dialysis patients. So, in a secularized climate as the Netherlands negative religious coping is still relevant.
The association between inflammatory markers and depressive symptoms has been extensively studied in chronic dialysis patients. However, the mechanism linking this association is not clear. Therefore, we examined in chapter 6 whether the association between inflammatory markers and depressive symptoms in chronic dialysis patients may be explained by tryptophan (TRP) degradation along the kynurenine (KYN) pathway. Indoleamine 2,3-dioxygenase (IDO) is the enzyme responsible for the degradation of TRP into KYN. TRP is a precursor of the neurotransmitter serotonin and a low concentration of serotonin has been associated with the development of depressive symptoms. Also, KYN degradation products may be associated with depressive symptoms. IDO is activated by inflammation and therefore, TRP degradation along the KYN pathway may be responsible for the association between inflammatory markers and depressive symptoms. In 490 chronic dialysis patients selected from the DIVERS study we examined the role of TRP degradation by adjusting the association between inflammatory markers and depressive symptoms for the KYN/TRP ratio. HsCRP and IL-6 were significantly associated with depressive symptoms. However, we did not find the expected role of TRP degradation. Although inflammatory markers were as expected significantly associated with a higher KYN/TRP ratio, which indicates that the activation of IDO is induced by inflammatory markers. Also, a significant association was found between a lower TRP concentration and more depressive symptoms, but this association was rather small and after adjustment for socio-demographics, lifestyle factors and medical variables the association lost significance. Therefore, TRP seems to have a small contribution in the onset of depressive symptoms, but other factors are likely to play a more important role. These results suggest that TRP degradation along the KYN pathway is not the link between inflammatory markers and depressive symptoms in chronic dialysis patients.

In chapter 7, we performed a longitudinal study in 513 chronic dialysis patients selected from the DIVERS study to examine long-term associations between inflammatory markers and depressive symptoms. In this way, also the direction of the inflammation-depression association may be explained. Cross-sectional associations between HsCRP and depressive symptoms were found at baseline and 6 months follow-up and between IL-1β and depressive symptoms at 6 months follow-up. No significant associations were found between inflammatory markers (HsCRP, IL-1β, IL-6, IL-10 and TNFα) at baseline and depressive symptoms at 6 and 12 months follow-up. Also no significant associations were found between depressive symptoms at baseline and inflammatory markers at 6 and 12 months follow-up. As a result, also the direction of the inflammation-depression association was not explained. Altogether, cross-sectional associations between inflammatory markers and depressive symptoms were found, but differed per measuring point. We found no evidence for longitudinal associations. Therefore, these results are more supportive for an associative rather than a causal relationship between inflammation and depressive symptoms in chronic dialysis patients.
In chapter 8 differences in the inflammation-depression and TRP-depression association between white and non-white chronic dialysis patients were examined. In 220 non-white chronic dialysis patients the presence of depressive symptoms was significantly higher compared to the presence in 270 white patients, namely 51% versus 37%. In the white patient group a significant association was found between HsCRP and depressive symptoms. In the non-white patient group a stronger significant association between HsCRP and depressive symptoms was found and also a significant association between IL-6 and depressive symptoms. TRP was only significantly associated with depressive symptoms in the non-white patient group. Therefore, racial differences in the association between inflammation and depressive symptoms and TRP and depressive symptoms exist. These results may also partly explain the higher prevalence of depressive symptoms in immigrant chronic dialysis patients. We also examined whether TRP degradation along the KYN pathway mediated the inflammation-depression association in those subgroups, but found no mediating role.

Finally, in chapter 9, the results of the performed studies in this thesis are summarized and discussed. First, we discussed the higher prevalence of depressive and anxiety symptoms found in immigrant compared to native (chronic dialysis) patients. This higher prevalence in immigrants has not been found in all countries. We found an especially high prevalence of depressive and anxiety symptoms in specific subgroups of patients. Therefore, these findings seem to differ per host country and immigrant population in the host country and no overarching conclusion regarding the effect of immigrant status on mental health can be drawn. All countries should select their immigrant subgroups at risk for the development of depressive and anxiety symptoms. Acculturation and biochemical parameters (inflammatory markers and tryptophan) seem to partly explain the higher prevalence of depressive and anxiety symptoms in immigrant chronic dialysis patients. Negative religious coping on the other hand, was both in native and immigrant patients strongly associated with depressive and anxiety symptoms and therefore appears to be still relevant in the secularized climate of the Netherlands. Second, the association between inflammatory markers and depressive symptoms is discussed. The cross-sectional associations found between inflammatory markers and depressive symptoms were somewhat inconsistent, which is also found in other studies among chronic dialysis patients. Explanations for these inconsistent results may be that this association is more pronounced in certain subgroups, as we found stronger associations in non-white chronic dialysis patients. Furthermore, inflammatory markers may be only associated with certain subtypes of depression, this should be examined in future studies. We found no evidence for longitudinal associations between inflammatory markers and depressive symptoms and no mediating role of TRP degradation in the cross-sectional association between inflammatory markers and depressive symptoms. Therefore, our results are more supportive for an associative rather than a causal relationship between inflammatory markers and depressive symptoms in chronic dialysis patients.