Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Depression, anxiety and quality of life of hemodialysis patients before and during the COVID-19 pandemic

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ABSTRACT

Objective: To investigate the impact of the coronavirus pandemic on mental health in hemodialysis patients, we assessed depression, anxiety and quality of life with valid mental health measures before and after the start of the pandemic.

Methods: Data were used from 121 hemodialysis patients from the ongoing prospective multicenter DIVERS-II study. COVID-19 related stress was measured with the Perceived Stress Scale – 10, depression with the Beck Depression Inventory – second edition (BDI-II)), anxiety with the Beck Anxiety Inventory (BAI) and quality of life with the Short Form – 12 (SF-12). Scores during the first and second COVID-19 wave in the Netherlands were compared to data prior to the pandemic with linear mixed models.

Results: No significant differences were found in BDI-II, BAI and SF-12 scores between before and during the pandemic. During the first wave, 33% of participants reported COVID-19 related stress and in the second wave 37%. These patients had higher stress levels (mean difference (MD) 4.7 (95%CI 1.5; 8.0), $p = 0.005$) and BDI-II scores (MD 4.9 (95%CI 0.7; 9.0), $p = 0.021$) and lower SF-12 mental component summary scores (MD -5.3 (95% CI -9.0, −1.6), $p = 0.006$) than patients who did not experienced COVID-19 stress. These differences were already present before the pandemic.

Conclusion: The COVID-19 pandemic does not seem to influence mental health in hemodialysis patients. However, a substantial subgroup of patients with pre-existent mental health problems may be more susceptible to experience COVID-19 related stress.

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1. Introduction

The impact of the coronavirus disease 2019 (COVID-19) pandemic on mental health among the general population becomes more evident as the pandemic is continuing. Previous studies show that symptoms of depression, anxiety and stress are common reactions to the COVID-19 pandemic [1–4]. Longitudinal studies report an increase of mental health problems compared to the pre-pandemic era [5–7]. Factors that may cause COVID-19 related stress are: fear of the contagious disease itself, loss of employment and financial insecurity, deaths of family members, friends, or colleagues, forced quarantine and social isolation [8]. Risk factors identified in published studies are female sex, younger or older age, previous psychiatric history, pre-existent physical or mental health problems, economic insecurity, and accompanying chronic disease including renal disease [9–13].

Only a limited number of studies investigating mental health during the COVID-19 pandemic among patients with chronic diseases have been performed. This is important as this group of patients are already vulnerable due to high levels of physical and mental distress. Indeed, in dialysis patients, symptoms of depression and anxiety are highly prevalent and associated with adverse clinical outcomes such as decreased quality of life, increased hospitalization and mortality [14–19]. Perceived stress during the COVID-19 pandemic could increase the burden of these symptoms in these patients.

Research investigating mental health problems in dialysis patients during the COVID-19 pandemic could therefore aid in assessing risk factors for and prevention of increased stress levels in these patients. The association between the COVID-19 pandemic and mental health problems in dialysis patients has been investigated in three studies, however, two studies did not compare results during the pandemic with pre-pandemic data [20–22]. Only the study by Bonenkamp and colleagues compared mental health before and during the COVID-19 pandemic and found no significant difference in mental health related quality of life (HRQoL) and mental health-related symptoms measured with single items from the Dialysis Symptom Index among peritoneal and hemodialysis patients during the COVID-19 pandemic compared to pre-pandemic data [20]. To the best of our knowledge, no studies have investigated the symptom severity of depression, anxiety and perceived stress in hemodialysis patients before and during the COVID-19 pandemic.

The aim of this article is first to investigate symptom levels of depression, anxiety and HRQoL in hemodialysis patients during the first and second wave of the COVID-19 pandemic compared to the pre-pandemic era. And second to explore whether depression, anxiety and HRQoL are associated to COVID-19 related stress.

2. Methods

2.1. Study design and participants

To compare depression, anxiety, quality of life and perceived stress in hemodialysis patients before and during the COVID-19 pandemic in both the first and second wave in the Netherlands, data were used from the ongoing multicenter prospective DIVERS-II study which consists of a randomized controlled trial (RCT) and a parallel observational cohort. The extensive study protocol has been published earlier [23]. In short, the RCT investigates the effectiveness of guided self-help problem solving therapy for depressive symptoms in hemodialysis patients. Inclusion criteria for the RCT were adult patients receiving maintenance hemodialysis (>90 days), who were able to fill out a questionnaire in Dutch and who had a depressive symptom score of 10 or higher on the Beck Depression Inventory – second edition (BDI-II) [24,25]. Patients who were excluded from the randomization because of a low score on the BDI-II or because of insufficient Dutch language skills, were offered to participate in a parallel observational cohort. In this parallel cohort, questionnaires were also available in Arabic, English and Turkish. The inclusion period of the total DIVERS-II study ran between January 8th,2018 and March 10th, 2020. Participants in both the trial and observational cohort were asked to fill out self-reported questionnaires on symptoms of depression, anxiety and HRQoL every three to six months, for a total follow-up period of 21 months. The study protocol, information brochure and informed consent were approved by the Medical Ethics Committee of MEC-U, the Netherlands (registration number: NL58520.100.17) and written informed consent was obtained from all participants before participation. This study is carried out in accordance with de declaration of Helsinki and was prospectively registered in the Dutch Trial Register (Trial NL6648).

For the present analysis, patients from the DIVERS-II RCT and observational cohort were included, if they completed a questionnaire during the first wave in the Netherlands, defined as the period between March 12th and July 1st, 2020. The second wave started on October 14th, 2020, and data-collection during the second wave includes only data from patients who were already included during the first wave. Data-collection for the present analysis ended on the first of March 2021. The second wave was still ongoing at the time of data-analysis. Questionnaires collected during the waves were compared with the last pre-wave questionnaires which had to have been supplied within 6 months before the first wave. Seventeen patients started the intervention of the RCT between September 2019 and March 2021, of which eleven patients were excluded because they were considered to be treatment-completers. A timeline of the data-collection is presented in Fig. 1.

2.2. Outcome measurements

The primary outcomes were the severity of symptoms of depression and anxiety, measured with the BDI-II and the Beck Anxiety Inventory (BAI), respectively [24–26]. Both questionnaires consist of 21 items each, in which respondents are asked how much these symptoms have bothered them in the past two weeks, on a scale ranging from 0 (not at all) to 3 (severely), with a total score between 0 and 63 where higher scores indicate more severe depression and anxiety. BDI-II and BAI scores were analyzed as continuous scores. Both the BDI-II and the BAI are validated in various cohorts of patients with chronic somatic diseases [26–28]. The minimum clinically important difference (MCID) in symptom score on the BDI-II and BAI which we used was a difference of at least 5 points [29].

The secondary outcome of HRQoL was measured with the Short Form-12 (SF-12), a validated questionnaire developed for patients with chronic conditions and frequently used in dialysis patients [30]. The SF-12 consists of a Mental Component Summary (MCS) score and a Physical Component Summary (PCS) score, on a scale of 0 to 100, where higher scores reflect better HRQoL [31]. We used a MCID of at least 5 points difference on PCS and MCS scores [32].

The secondary outcome of COVID-19 related stress was measured during the pandemic by the Perceived Stress Scale-10 (PSS-10). This is a widely used and validated questionnaire which measures the global levels of stress in the last month by asking to which degree persons find their lives unpredictable, uncontrollable and overloaded [33,34]. The Dutch version of the PSS-10 translated by the Longitudinal Aging Study Amsterdam (LASA) was used [35]. The 10 questions were answered on a five point Likert scale from ‘never’ (0) to ‘very often’ (4), with a total score between 0 and 40. The scale consists of six negatively worded items and four positively worded items, from which a negative subscale with a score between 0 and 24 and a positive subscale with a score between 0 and 16 can be calculated. We consider 4 points difference as MCID [36]. To determine if perceived stress was related to COVID-19, the following question was added to the PSS-10: “In the last month, how often have you felt that the tensions or ‘stress’, as answered by you in the above questions, were caused by the corona outbreak?” If patients answered ‘never’ or ‘almost never’, their stress was considered COVID-19 unrelated. Patients who answered ‘sometimes’, ‘fairly often’ of ‘very often’ were considered to experience COVID-19 related stress.

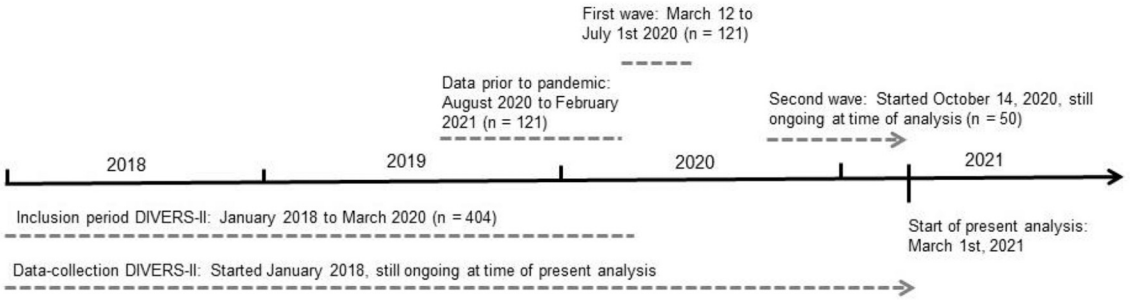

Fig. 1. Timeline of data collection DIVERS-II study and present analysis.

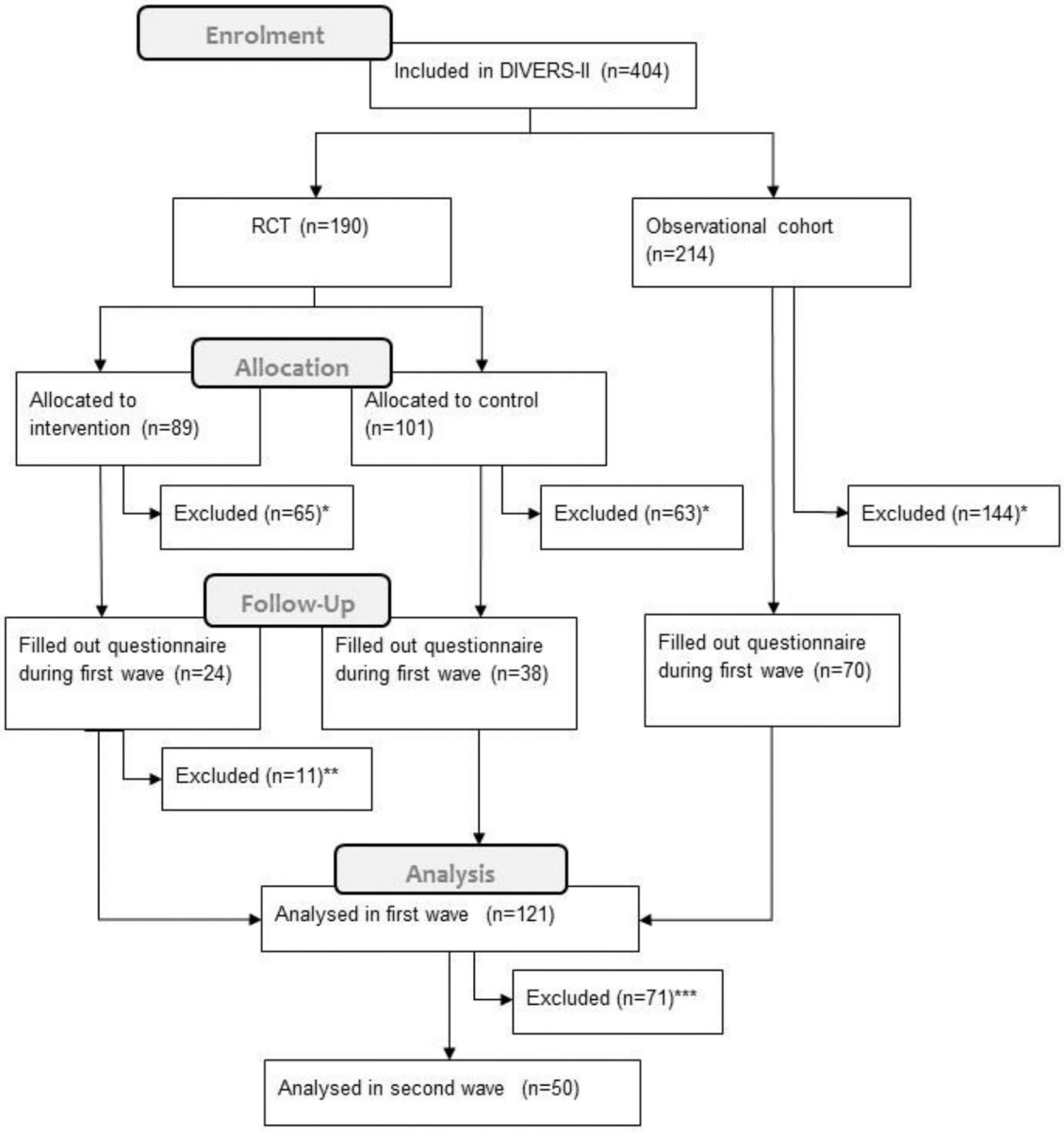

Fig. 2. Flow diagram.
*Excluded because no questionnaire was filled out during the first wave.
**Excluded because intervention was not completed before study period.
***Reasons for exclusion: Did not send questionnaire back in time ($n = 18$), completed follow-up in first wave ($n = 15$), questionnaire planned between waves (n = 12), lost to follow up ($n = 11$), questionnaire planned after study period ($n = 8$), died ($n = 7$).
Abbreviations: RCT, randomized controlled trial.

2.3. Data collection

At baseline, sociodemographic and clinical data were collected through self-reported questionnaires and electronic patient files. The primary cause of kidney disease was classified according to the European Renal Association–European Dialysis and Transplant Association (ERA-EDTA) coding system and divided into four groups (renal vascular disease, diabetic nephropathy, glomerulonephritis and other) [37]. The Davies comorbidity index was used to define the level of comorbidity [38]. This index is based on the presence or absence of seven comorbid conditions, where patients without comorbidities are classified as low risk, with one or two comorbidities as medium risk and with three or more comorbidities as high risk. Follow-up data on COVID-19 PCR test results and COVID-19 related hospitalization and mortality was extracted from electronic patient files.

2.4. Statistical analysis

Standard descriptive statistics were used to present baseline characteristics. Differences in continuous scores of the BDI-II, BAI and SF-12 before the COVID-19 pandemic and during both waves were analyzed with linear mixed model analysis, adjusted for age, sex, immigrant status, high formal education, dialysis vintage and high comorbidity score. Effects of individual confounders on the outcomes were analyzed in univariate mixed model analysis. Sensitivity analysis was performed excluding all patients from the intervention group of the RCT to assess treatment effect on the outcomes. PSS-10 total score and positive and negative subscales in patients with COVID-19 related stress were compared to the scores of patients without COVID-19 related stress with linear regression analysis, adjusted for age, sex, immigrant status and high comorbidity score. BDI-II, BAI and SF-12 scores of patients with COVID-19 related stress and COVID-19 unrelated stress were compared with linear mixed model analysis, adjusted for age, sex, immigrant status, high formal education, dialysis vintage and high comorbidity score. The Bonferroni method was used to adjust for multiple comparison. For the primary outcomes depression and anxiety, a significance level of $\alpha < 0.025$ was used.

2.5. Missing values

To assess the impact of missing values on results, missing BDI-II, BAI and SF-12 items of 121 patients before and during the first wave and of 50 patients in the second wave were imputed by using multiple imputation techniques (10 repetitions) as a sensitivity analysis. All statistical analyses were performed using SPSS for Windows, version 22 (IBM Corp).

3. Results

The patient flow is presented in Fig. 2. A total of 121 patients were included in the analysis of the first wave and 50 patients in the analysis of the second wave. Baseline characteristics are summarized in Table 1. The majority of the patients were male (69%), mean age was 67 years, median dialysis vintage was 23 months and 10% of the patients had a history of depression.

In the first wave, a SARS-CoV-2 PCR test was performed in 23 of 121 patients of which none tested positive. Two patients were admitted to the hospital with a suspected COVID-19 infection, but test results were negative. In the second wave, a PCR was performed in 13 out of 50 patients of which five (10%) tested positive for SARS-CoV-2. One patient was admitted to the hospital for three days and one patient was admitted to a nursing home for 20 days because care options at home were insufficient. No COVID-19 related mortality was reported in this cohort during the study period.

No significant differences in BDI-II and BAI scores were found with mixed model analysis adjusted for predefined confounders, between the measurements up to six months before COVID-19 and during the first and second wave (Table 2). Univariate analysis showed a higher BDI score of 4.4 points (95%CI 0.5;8.2, $p = 0.03$) and a BAI score of 5.9 points (95%CI 2.5;9.3, $p = 0.001$) in women compared to men, independent of time effect. The effect of sex on HRQoL was seen only in the MCS score, where women scored 5.3 (95%CI 1.7; 8.8, $p = 0.004$) points lower than men. No significant differences were found in univariate analysis of the other confounders. Sensitivity analysis excluding all patients from the intervention group of the RCT showed no major differences.

During the first wave, 33% of the participants reported that the stress they experienced was caused by the COVID-19 pandemic. During the second wave this was 37%. Participants who reported that their perceived stress was caused by the pandemic, scored 4.7 points higher on the PSS-10 during the first wave compared to participants who

Table 1
Patient characteristics of 121 participating hemodialysis patients at baseline.

Characteristic	All patients (n = 121)
Demographic	
Age (year)	67 ± 13
Male sex	84 (69%)
Immigrant*	44 (36%)
Country of birth	
European	86 (71%)
South America/Caribbean	17 (14%)
Southern Asia/South Eastern Asia	10 (8%)
Sub Saharan Africa	5 (4%)
Northern Africa	3 (3%)
Social	
Married	54 (45%)
Has Children	91 (75%)
Education**	
Low	44 (36%)
Middle	48 (40%)
High	29 (24%)
Not employed	106 (88%)
Renal and dialysis	
Dialysis vintage (months)	23 [9–42]
Primary kidney disease	
Renal vascular disease	30 (25%)
Diabetic nephropathy	36 (30%)
Glomerulonephritis	9 (7%)
Other	46 (38%)
Kt/V_{urea} at baseline	3.6 ± 1.2
Residual diuresis of ≥100 ml/24 h	83 (69%)
On waiting list for kidney transplant	
Yes	33 (27%)
No, for medical reasons	74 (61%)
No, by patient preference	14 (12%)
Clinical	
Davies comorbidity index***	
Low comorbidity	22 (18%)
Medium comorbidity	82 (68%)
High comorbidity	17 (14%)
Comorbid conditions	
Diabetes mellitus	63 (52%)
Cardiovascular disease and hypertension****	101 (84%)
Psychiatric	
Current psychotherapy	5 (4%)
History of depressive disorder	12 (10%)
History of anxiety disorder	0 (0%)

Note: Values are presented as mean ± standard deviation, median [interquartile range], or frequency (percentage).

* Immigrant status is based on country of birth of both patient and biological parents of patient.

** Education: Low = primary education, middle = secondary education, high = higher professional education and university.

*** Davies comorbidity index: low = no comorbidities, medium = one or two comorbidities, high = three or more comorbidities.

**** CVD = acute coronary syndrome, angina pectoris, percutaneous coronary angioplasty, coronary artery bypass surgery, heart failure, peripheral arterial vascular disease, stroke.

Table 2
Depression, anxiety and health related quality of life scores before the COVID-19 pandemic and during the first and second wave.

	Pre-pandemic	First wave	Mean difference (95% CI)*	*p*-value	Second wave	Mean difference (95% CI)*	p-value
Depression							
BDI-II	10.4 ± 8.5	9.8 ± 8.3	−0.9 (−2.0; 0.1)	0.09	9.1 ± 8.9	0.2 (−1.3; 1.7)	0.79
Anxiety							
BAI	8.7 ± 8.6	8.0 ± 7.9	−1.0 (−2.5; 0.6)	0.21	7.9 ± 7.5	−0.7 (−2.8; 1.4)	0.51
HRQoL							
SF-12 PCS	37.2 ± 9.7	37.3 ± 9.3	0.37 (−2.1; 2.8)	0.76	36.1 ± 10.6	0.8 (−2.5; 4.2)	0.62
SF-12 MCS	54.0 ± 9.0	53.9 ± 8.8	0.1 (−1.7; 2.0)	0.88	53.6 ± 9.2	−0.2 (−2.8; 2.4)	0.86

Note: Values are presented as mean ± standard deviation.
Note: Pre-pandemic and during first wave $n = 121$, during second wave $n = 50$.
Abbreviations: COVID-19, Corona virus disease 2019; CI, confidence interval; BDI-II; Beck Depression Inventory – Second edition, BAI; Back Anxiety Inventory, HRQoL, health related quality of life; SF-12, 12-Item Short Form Health Survey; PCS, Physical Component Summary; MCS, Mental Component Summary.
* Analyzed with a linear mixed model, adjusted for age, sex, immigrant status, high formal education, dialysis vintage and high comorbidity score.

reported their stress was unrelated to COVID-19 (95%CI 1.5; 8.0, $p = 0.005$) (Table 3, Fig. 3). In the second wave this difference was 7.2 points (95%CI 2.7; 11.7, $p = 0.003$). This difference is explained largely by a significant difference on the negative subscale, which consists of questions on being upset about unexpected things, unable to control important things in life, feeling nervous and stressed, not being able to cope with things you have to do, feeling angry about things outside of your control and not being able to overcome difficulties.

Participants who reported to experience COVID-19 related stress, scored 4.9 points higher on the BDI-II (95% CI 0.7; 9.0, $p = 0.02$) and 5.3 points lower on the MCS of the SF-12 (−9.0, −1.6, $p = 0.006$) than participants with COVID-19 unrelated stress both before and during the pandemic in a mixed model analysis adjusted for confounders (Table 4).

3.1. Missing values

Baseline demographic and clinical variables were missing in 0.4% of the cases. The overall percentage of missing questions in the first wave on the BDI-II, BAI and SF-12 was <5%. The PSS-10 was filled out by 73 patients in the first wave an 40 patients in the second wave. Sensitivity analysis, using multiple imputation of missing items, showed no substantial differences compared to the complete case analysis.

Table 3
Perceived stress scores in hemodialysis patients during the first and the second COVID-19 wave.

First wave PSS-10	Perceived stress in total group	Stress related to COVID-19	Stress not related to COVID-19	Mean difference (95% CI)*	*P*-value
Overall score	11.0 ± 6.4	14.2 ± 5.9	9.3 ± 5.7	4.7 (1.5; 8.0)	**0.005**
Positive subscale	6.9 ± 4.3	6.7 ± 6.7	6.4 ± 4.3	0.4 (−1.9; 2.7)	0.76
Negative subscale	4.1 ± 4.1	7.5 ± 4.8	2.9 ± 3.9	4.4 (2.1; 6.7)	**<0.001**
Second wave PSS-10					
Overall score	11.7 ± 7.6	15.5 ± 8.2	9.4 ± 6.6	7.2 (2.7; 11.7)	**0.003**
Positive subscale	6.0 ± 3.7	6.2 ± 3.3	5.8 ± 4.1	1.2 (−3.0; 5.2)	0.58
Negative subscale	5.6 ± 5.5	9.3 ± 6.9	3.6 ± 3.5	6.1 (2.0; 10.2)	**0.006**

Note: Values are presented as mean ± standard deviation.
Note: Before the pandemic and during the first wave COVID-19 related stress $n = 24$ and COVID-19 unrelated stress $n = 49$. During the second wave COVID-19 related stress $n = 15$ and COVID-19 unrelated stress $n = 25$.
Abbreviations: PSS-10, perceived stress scale – 10; HD, hemodialysis; COVID-19, Corona virus disease 2019; CI, confidence interval. P-values given in bold are considered statistically significant ($\alpha < 0.025$)
* Analyzed with a linear regression model, adjusted for age, sex, immigrant status and high comorbidity score.

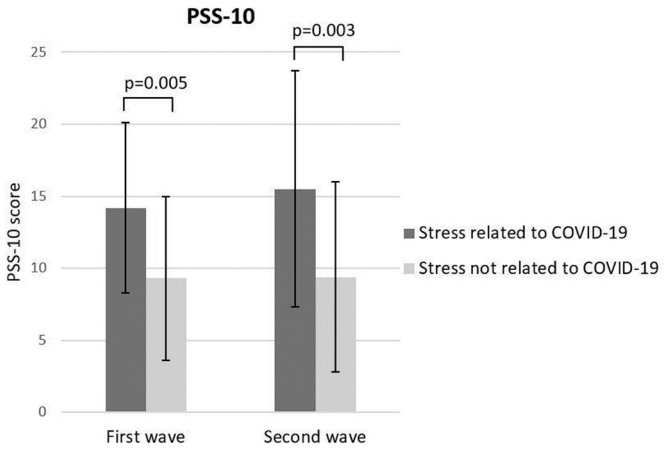

Fig. 3. Bar chart of difference in perceived stress scores of patients with COVID-19 related stress and COVID-19 unrelated stress during the first and second COVID-19 wave.
Note: Values are presented as mean ± standard deviation.
Abbreviations: PSS-10, Perceived Stress Scale – 10; COVID-19, Corona virus disease 2019.

4. Discussion

This study aimed to investigate depression, anxiety and HRQoL in hemodialysis patients during the COVID-19 pandemic compared to the pre-pandemic era and to explore whether depression, anxiety and HRQoL are related to COVID-19 related stress. Overall, no clinically significant differences in severity of symptom levels of depression, anxiety and HRQoL in hemodialysis patients were found between the pre-pandemic era and during the first and second COVID-19 wave in the Netherlands. We did find higher levels of depression and anxiety and lower mental health related quality of life scores in women than in men, which is consistent with literature from the general population [9–11,13,39]. Importantly, we found that high depression, anxiety and HRQoL scores were already pre-existent in hemodialysis patients before the COVID-19 outbreak.

Cross-sectional studies in dialysis patients during COVID-19 without comparison to pre-pandemic data show a prevalence of depression of 22–27% and a prevalence of anxiety of 12%, but these scores are difficult to interpret as symptoms of depression and anxiety were already highly prevalent in dialysis cohorts before the pandemic [21,22]. Our findings are in concordance with the only other prospective study in 177 dialysis patients by Bonenkamp and colleagues, which compared mental health related symptoms measured with single items from the Dialysis

Table 4
Depression, anxiety and health related quality of life scores of patients with COVID-19 related stress and COVID-19 unrelated stress before the COVID-19 pandemic and during the first and the second wave.

	Stress related to COVID-19	Stress not related to COVID-19	Mean difference (95% CI)*	P-value
BDI-II				
Before COVID-19	13.3 ± 9.2	8.5 ± 7.1	4.9 (0.7; 9.0)	**0.021**
During first wave	12.6 ± 9.0	7.4 ± 7.4		
During second wave	13.7 ± 7.8	7.8 ± 7.8		
BAI				
Before COVID-19	12.1 ± 9.7	6.9 ± 6.9	2.9 (0.6; 6.3)	0.11
During first wave	10.5 ± 7.8	6.0 ± 6.0		
During second wave	12.5 ± 9.6	6.4 ± 6.1		
SF-12 - PCS				
Before COVID-19	35.6 ± 8.9	38.6 ± 10.2	−2.3 (−6.8; 2.2)	0.31
During first wave	35.9 ± 9.9	38.9 ± 9.0		
During second wave	34.5 ± 10.6	36.5 ± 11.9		
SF-12 - MCS				
Before COVID-19	50.2 ± 9.2	56.4 ± 8.3	−5.3 (−9.0, −1.6)	**0.006**
During first wave	48.9 ± 8.5	56.8 ± 7.0		
During second wave	46.3 ± 11.0	55.6 ± 7.4		

Note: Values are presented as mean ± standard deviation.
Note: Before the pandemic and during the first wave COVID-19 related stress n = 24 and COVID-19 unrelated stress n = 49. During the second wave COVID-19 related stress n = 15 and COVID-19 unrelated stress n = 25.
Abbreviations: COVID-19, Corona virus disease 2019; CI, confidence interval; BDI-II; Beck Depression Inventory – Second edition, BAI; Back Anxiety Inventory, SF-12, 12-Item Short Form Health Survey; PCS, Physical Component Summary; MCS, Mental Component Summary. P-values given in bold are considered statistically significant ($\alpha < 0.025$).
* Analyzed with a linear mixed model, adjusted for age, sex, immigrant status, high formal education, dialysis vintage and high comorbidity score.

Symptom Index and HRQoL with the SF-12 before and during the pandemic, who also found no evidence for increase of mental health problems during the pandemic [20]. In addition, we used valid and more detailed mental health measures specifically for measuring depression and anxiety. A possible explanation for the lack of influence of COVID-19 on symptom levels of depression and anxiety in hemodialysis patients could be the fact that their daily lives did not change as much as the lives of the general population during the wave since in-center hemodialysis care was continued unchanged. The high prevalence of depression and anxiety before the pandemic may also be responsible for a diminished effect of a pandemic on mental wellbeing.

In our cohort, one third of all hemodialysis patients reported COVID-19 related stress. These patients had more severe symptoms of depression and lower mental health related quality of life both before and during the pandemic compared to participants who reported their stress to be unrelated to COVID-19. There was no difference between participants with COVID-19 related stress and participants with COVID-19 unrelated stress on severity of symptoms of anxiety and physical health related quality of life. These findings suggest that hemodialysis patients with more severe symptoms of depression and lower levels of mental health related quality of life prior to the COVID-19 pandemic, are more susceptible to experience stress caused by the pandemic.

Meta-analyses on self-reported stress among the general population during the COVID-19 pandemic demonstrated similar results (30–40%) [2,3]. In a cross sectional study, 31% of hemodialysis patients experienced high levels of stress during the COVID-19 pandemic using a cut off of ≥6 on the PSS-4 [21]. We found an even higher prevalence of high stress levels of 38–39% in our cohort using the same cut off score in these four questions from the PSS-10. Although our study does not provide insight in specific reasons for perceived stress during the COVID-19 pandemic, other studies from dialysis populations report that 85% of hemodialysis patients were worried about the risk of infection during the hemodialysis treatment and the transportation to the hospital, and 38% of peritoneal dialysis patients reported that their life was affected by the COVID-19 pandemic because they experienced restriction of activity, fear and panic, restricted hospital access and social isolation [21,22]. Mortality rates of COVID-19 are known to be higher among patients with pre-existing kidney diseases compared to individuals without pre-existing kidney diseases [40,41]. It has been reported that this is one of the reasons that a substantial part of the dialysis patients experiences fear of COVID-19 [20–22]. In our cohort, none of the hemodialysis patients were diagnosed with COVID-19 during the first wave and 10% during the second wave. However, observing COVID-19 related disease and mortality of fellow-patients might increase stress in hemodialysis patients.

4.1. Strengths & limitations

This study has several strengths. First, we compared data on depressive and anxiety symptoms measured with validated questionnaires during the pandemic with data of the pre-pandemic era in hemodialysis patients. Second, this is the first prospective study that reports mental health in hemodialysis patients with additional data from the second wave. This provides longitudinal information about the development of mental health problems during the COVID-19 pandemic in hemodialysis patients. Lastly, we used data from a large multicenter cohort study in the Netherlands, which increases generalizability.

This study has several limitations. First, we have a relatively small sample size of 121 patients in the first wave and an even smaller sample size of 50 patients in the second wave. This is comparable to the current literature on COVID-19 related mental health in dialysis patients with sample sizes of 49 to 177 patients. [20–22] Also, as the upper levels of the 95% confidence intervals we found are still lower than the MCID, it is unlikely that with a larger sample size a clinically relevant difference will be found. Second, selection bias might have occurred since this cohort included patients from an RCT which may play a role in which patients were willing to participate. To address this issue, we offered patients the opportunity to participate in a parallel observational cohort if patients were not willing or motivated to participate in an interventional study. To limit the effect of the intervention on the outcomes of this study, we excluded patients who completed the intervention during the period of the present study from the analysis and performed sensitivity analysis excluding all patients from the intervention group. Third, we were not able to compare perceived stress during COVID-19 with pre-pandemic data since the PSS-10 is not part of the original DIVERS-II protocol. Fourth, although the MCID has been used and validated in other chronically ill patient groups, it has not been validated in the dialysis population [42]. Finally, our low infection rate in the first wave and low COVID-19 related mortality rate could decrease generalizability as currently reported COVID-19 infection rates in the hemodialysis population are 3–6% and COVID-19 mortality rates are up to 25% [40,41,43,44].

5. Conclusion

In conclusion, the COVID-19 pandemic does not seem to influence severity of symptoms of depression, anxiety and quality of life in

hemodialysis patients during the first and second COVID-19 wave in the Netherlands, compared to pre-pandemic data. However, a substantial subgroup of patients with pre-existent higher symptom levels of depression and lower mental health related quality of life may be more susceptible to experience COVID-19 related stress. This underscores the need for screening and treatment of depression and mental health related quality of life in hemodialysis patients to prevent increase of stress symptoms in this group during pandemics and other major stressful events in the future.

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Declarations of interest

The authors have no competing interests to report.

Authors' contributions

EN, RWS, FWD, PvO, CEHS and BFPB have contributed to the study design and all authors have contributed to the preparation of this manuscript. EN, NR, YS, PCS, LJV, MJED, MW, EH, WJWB, MS, KF and CEHS included the patients and contributed to data acquisition. EN performed the statistical analysis under supervision of RWS and FWD. EN and NR wrote the first draft of this manuscript; all co-authors critically reviewed and revised the initial draft and approved the final version of the manuscript.

Data availability statement

The data underlying this article cannot be shared publicly for the privacy of individuals that participated in the study. The data will be shared on reasonable request to the corresponding author.

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