Prevalence and Association of Pruritus and its Current Treatment during the First Year of Dialysis

A Dutch Nocturnal and Home Dialysis Study to Improve Clinical Outcomes Study

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Key Points

- Incident dialysis patients show a high prevalence of pruritus during the first year of dialysis, with pruritus being either persistent or fluctuating.
- Medical treatment for pruritus does not improve quality of life within the 25% of patients with pruritus receiving it.
- High prevalence, negative effect, and low treatment rate of pruritus urges for more awareness, for instance, by the means of patient reported outcomes.

Abstract

Background Pruritus is common in dialysis patients and associated with impaired health-related quality of life (HRQoL) and sleep disturbances. Its pathophysiology remains unclear, resulting in limited treatment options and lack of treatment guidelines. The exact trajectory of pruritus after dialysis initiation, nor the state of current medical treatment, has been studied.

Methods Incident dialysis patients (N=1438) included in the Dutch nocturnal and home dialysis study to improve clinical outcomes were studied. Outcome parameters were prevalence of pruritus, severity of pruritus, and the use of antipruritic medication, repeatedly measured during the first year of dialysis. Associations between treatment, pruritus, and quality of life were longitudinally studied using linear mixed models.

Results The prevalence of pruritus ranged from 50.5% to 56.6% during the first year of dialysis. Throughout the year, approximately 35% experienced persistent pruritus and 40% fluctuating pruritus. During follow-up, 21.5%–26.5% received medical treatment for pruritus. Emollients were associated with more severe pruritus (adjusted β=0.31; 95% confidence interval [CI], 0.15 to 0.48); the remaining treatments did not show any association. Pruritus was significantly associated with lower physical and mental HRQoL (adjusted β=−2.04; 95% CI, −2.78 to −1.30 and β=−1.73; 95% CI, −2.51 to −0.94, respectively), irrespective of treatment.

Conclusions During the first year of dialysis, pruritus is highly prevalent, predominantly fluctuating, and associated with impaired HRQoL. The minority of patients received medical treatment; in our study, current treatment was not associated with an improvement of pruritus. These results highlight the need for more awareness among clinicians and for the development of effective treatment options.

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Introduction

Although the first reference of pruritus, commonly known as itching, can be traced back to an ancient Egyptian medical papyrus dating to the 19th century BC, it was not until 1874 that Rosenstein established a connection between uncontrollable itching without skin lesions and uremic kidney disease.[1,2] This condition was subsequently denoted as uremic pruritus. Nowadays, the nomenclature CKD-associated pruritus is considered more precise because it reflects the current perspective that there is no direct causal relationship between uremia itself and pruritus.[3]

CKD-associated pruritus, or pruritus for short, is common among maintenance dialysis patients, with most studies reporting prevalences around 50%.[4,5] This high prevalence is accompanied by a negative effect on health-related quality of life (HRQoL) and an increase in depressive symptoms.[6–8] In addition, these patients often show an increase in sleep-related problems, like restless legs and difficulty falling asleep.[9,10]

While the negative consequences of pruritus are well-documented, the underlying pathophysiology remains largely unclear. It is hypothesized to involve a complex interaction between the skins, biology, opioid pathways within the nervous system, and dysfunction of inflammatory mediators within the immune system.[11,12] The lack of clarity concerning the pathophysiology could have contributed to the absence of well-studied effective treatments for patients experiencing pruritus and clear therapeutic guidelines for their clinicians. Several medical and nonmedical therapeutic options have been investigated through multiple observational studies and trials. Often, these studies display varying quality due to small sample sizes, absence of blinding, and short treatment windows, thus resulting in weak evidence. Overall, these treatments generally show limited effectiveness in relieving dialysis patients from pruritus.[13–16]

Currently, the lack of clear guidelines has contributed to a wide range of potentially effective treatment options, creating significant uncertainty regarding the standardized care for dialysis patients with pruritus. Furthermore, there is a lack of longitudinal studies giving better insight in the trajectory and severity of pruritus and its treatment. In addition, previous studies mainly focused on prevalent dialysis patients, resulting in a heterogenous study population and limited information on the trajectory of pruritus during the first year of dialysis. Finally, peritoneal dialysis patients are often not included in analyses, with focus being primarily on hemodialysis patients. Therefore, the aim of this study was to investigate the impact of pruritus and its treatment among incident dialysis patients during their first year of dialysis treatment. This will be investigated by assessing the prevalence and severity, exploring its current treatment, and looking into the longitudinal association between treatment, pruritus, and HRQoL.

Methods

Study Design and Population

Data were obtained from the Dutch nOcturnal and hoME dialysis Study To Improve Clinical Outcomes (DOMESTICO), a multicenter, observational cohort study conducted in 59 participating dialysis centers across The Netherlands and Belgium.[17] In this study, HRQoL and clinical outcomes of patients on home dialysis are compared with those of patients on in-center dialysis. All patients aged 18 years or older with kidney failure who started maintenance dialysis were eligible for inclusion. To prevent selection bias, patients who were missed for inclusion at dialysis initiation were allowed to be included at 3 months after initiation. For this study, patients who filled out at least two questionnaires were included.

Patients with a kidney transplantation within 3 months after starting dialysis or a life expectancy less than 3 months were excluded. Inclusion in DOMESTICO started in December 2017 and ended in December 2022. The minimum duration of follow-up was 1 year, and the final follow-up of the study ended in December 2023.

All patients included provided written informed consent on enrollment. Ethical approval was obtained from the medical research ethics committee of the VU University Medical Center Amsterdam (no.: NL63277.029.17). The study is conducted according to the principles of the Declaration of Helsinki. The DOMESTICO study is registered in the Dutch Trial Register (no: NL6519). We reported our results in accordance with the STrengthening the Reporting of OBservational studies in Epidemiology guidelines (Supplemental Table 1).[18]

Measurements and Data Collection

For this study, data from the DOMESTICO study were collected at baseline, 3, 6, and 12 months after the start of dialysis. At baseline, data were collected on demographic characteristics and comorbidity. During each visit, dialysis-specific characteristics, medication, laboratory results, and questionnaires were collected. The presence and severity of pruritus was measured using the Dialysis Symptom Index (DSI) questionnaire. The DSI is a symptom assessment instrument to describe the presence and severity of dialysis-specific symptoms, consisting of 30 items on both physical and mental dialysis-related symptoms. The severity of each symptom is reported using a five-point Likert scale, ranging from 1 (no pruritus) to 5 (severe pruritus).[19]

Data on medication were retrieved from electronic patient files. Because there is a lack of internationally accepted guidelines on pruritus treatment in dialysis patients, treatment was subscribed either based on common practice in Dutch and Belgian dialysis centers or on previous studies on the treatment of pruritus.[16,20,21] An overview of all included medications and corresponding classes are listed in Supplemental Table 2.

To measure HRQoL, the 12-item short form health survey was used.[22] The 12-item short form health survey consists of 12 questions that contribute to two component scores, namely the physical component summary (PCS) score, reflecting physical HRQoL, and the mental component summary (MCS) score, reflecting mental HRQoL. These component scores range from 0 to 100, with higher scores indicating better mental and physical HRQoL. In the general population, a score around 50 is found for both the PCS and MCS score.[23]

Statistical Analyses

Baseline characteristics were presented for all included patients. Continuous variables were presented as mean with SD and as median with interquartile range in case of skewed distribution. Categorical variables were presented as numbers with percentages. Descriptive information on the prevalence and the severity of pruritus were presented graphically (and as percentages with a 95% confidence interval [CI]). Descriptive data on the different treatments used per medication class for pruritus were presented as numbers with percentages at every study visit.

Longitudinal analyses were all performed using linear mixed models (LMMs). In the first analysis, overall treatment was used as a categorical independent variable. In the second and third analysis, topical and systemic treatment were analyzed separately as categorical independent variables containing the corresponding medication classes. For the analysis investigating the association between pruritus and HRQoL, both physical and mental HRQoL were used as continuous dependent variables. All analyses were performed unadjusted and adjusted for potential confounders. For the association between treatment and pruritus, the following confounders were included: age, sex, dialysis modality at baseline, pruritus-associated comorbidity, and the presence of dry skin at baseline. To prevent regression to the mean, the severity of pruritus on baseline was also included in the model.[24] Because treatment was time-dependent, time was included as a fixed effect to prevent possible confounding by time. Finally, for the analyses with topical and systemic treatment, concomitant treatment with systemic or topical treatment, respectively, were added to the model. For the association between pruritus and HRQoL, the following confounders were included: age, sex, modality at baseline, primary kidney disease, and kidney transplantation in the past. To assess the influence of treatment of pruritus on the association between pruritus and HRQoL, the presence of treatment was added as interaction term. A significant interaction term implies effect modification, meaning a different association between pruritus and HRQoL for patients with and without treatment.[25]

Missing values were assumed missing at random. Under the missing at random assumption, LMM are able to handle missing values. Therefore, additional imputation of missing values was considered not necessary.[26] Although LMM can handle missing values, drop-out due to death and kidney transplantation could truncate the outcome.[27] Therefore, sensitivity analyses were performed to ensure the robustness of the longitudinal results. The analyses were repeated without the patients who dropped out.

All analyses were performed using SPSS version 28.0 (IBM, Armonk, NY) and R (version 4.2.1). The results of the longitudinal analyses were reported with a 95% CI or a P value for statistical significance. A P value of <0.05 was considered significant.

Results

Baseline Characteristics

A total of 1438 patients filled out at least two questionnaires during follow-up and were included. Table 1 presents the characteristics of all included patients. The mean age of all patients was 65 (±14) years at the time of inclusion, and most of the patients was male (66%). Approximately three-quarters of the patients (76%) started on hemodialysis. A third of the included patients (31%) had a pruritus-associated comorbidity, with previous malignancy and systemic disease as the most prevalent. During the follow-up period of 1 year after start of dialysis, a total of 117 patients (8%) received a kidney transplant and 59 patients (4%) died.

Prevalence and Severity of Pruritus

Figure 1 shows the prevalence of pruritus at each study visit and its trajectory during the 1-year follow-up. The prevalence of pruritus ranged from 50.5% to 56.6% during the first year of dialysis. Throughout this first year of dialysis, 24.3% (95% CI, 22.1 to 26.5) of the patients who never experienced pruritus, 33.4% (95% CI, 31.0 to 35.8) had persistent pruritus, and 42.3% (95% CI, 39.7 to 44.9) had fluctuating pruritus. The distribution of the severity of pruritus over time is shown in Figure 2. During that first year of dialysis, 74.8% of patients undergoing hemodialysis experienced pruritus at least once, compared with 78.2% of those receiving peritoneal dialysis ($P = 0.20$). Hemodialysis patients without pruritus had a mean urea reduction rate of 60.7% and patients with pruritus, a rate of 59.7%, which did not significantly differ ($P = 0.19$).

Current Treatment of Pruritus

A total of 999 patients had at least one available medication list during the study. Table 2 shows descriptive information on the treatment of pruritus. A minority of the patients received treatment for pruritus, ranging from 21.5% to 26.5%. Patients were either treated topically, systemically, or received a combination of topical and systemic treatment. Most patients received only one antipruritic agent. Emollients were the most frequently prescribed topical treatment, ranging from prescriptions in 8.6%–10.1% of patients, followed by topical corticosteroids, ranging from 5.5% to 6.6%. Antihistamines were the most commonly prescribed systemic treatment, ranging from 6.1% to 6.6%, followed by gabapentinoids, ranging from 4.0% to 7.6%.

Association between Treatment and Pruritus Severity

Results of the longitudinal analyses are shown in Table 3. The β-coefficient reflects the change in severity of pruritus on a five-point Likert scale compared with the reference, being no treatment. After adjustment for confounders, the use of both topical treatment ($\beta=0.14$; 95% CI, 0.02 to 0.27) and the combined treatment ($\beta=0.36$; 95% CI, 0.16 to 0.57) were associated with more severe pruritus over the follow-up period compared with no treatment. There was no significant association between the use of systemic treatment and the severity of pruritus compared with no treatment.

Within the group of topical treatments, only emollients ($\beta=0.31$; 95% CI, 0.15 to 0.48) were associated with more severe pruritus compared with no treatment. All different agents within the systemic treatment group did not show a significant association with severity of pruritus compared with no treatment.

Table 1. Characteristics at dialysis initiation

Characteristics	Total Incident Patients (N=1438)
Age (yr), mean (SD)	64.5 (14.0)
Sex, female, *n* (%)	483 (33.6)
Primary kidney disease, *n* (%)	
Diabetic kidney disease	237 (16.5)
GN	176 (12.2)
Polycystic kidney disease	81 (5.6)
Pyelonephritis, interstitial nephritis or urolithiasis	67 (4.7)
Renovascular disease	346 (24.1)
Other or unknown	531 (36.9)
Charlson comorbidity index, median (IQR)	3 (2–5)
Pruritus-associated comorbidity, *n* (%)	
Liver disease	34 (2.5)
Previous malignancy	210 (15.4)
Systemic disease	196 (14.4)
Previous kidney transplant, *n* (%)	129 (10.3)
Dialysis modality at start, *n* (%)	
Hemodialysis[a]	1089 (75.7)
Peritoneal dialysis	349 (24.3)
Acute start of dialysis, *n* (%)	228 (15.7)
eGFR at dialysis initiation (ml/min per 1.73 m^2), median (IQR)[b]	6.8 (0.0–9.4)
Residual diuresis (>100 ml/d), *n* (%)	776 (72.4)
Serum urea level (mg/dl), mean (SD)	175.9 (70.4)
Serum calcium (mg/dl), mean (SD)	9.1 (0.9)
Serum phosphate level (mg/dl), mean (SD)	5.2 (1.6)
Calcium×phosphate product (mg^2/dl^2), mean (SD)	46.8 (14.4)
Serum PTH level (pg/dl), mean (SD)	384 (363)
Serum albumin (g/dl), mean (SD)	3.6 (0.6)
Serum hemoglobin (g/dl), mean (SD)	10.8 (1.5)
HRQoL (SF-12), mean (SD)	
Physical component score	36.0 (10.0)
Mental component score	47.0 (10.1)

Missing values: Charlson Comorbidity Index, n=126 (8.8%); pruritus-associated comorbidity: liver disease, n=81 (5.6%); pruritus-associated comorbidity: previous malignancy, n=74 (5.1%); pruritus-associated comorbidity: systemic disease, n=80 (5.6%); eGFR at dialysis initiation, n=400 (27.8%); residual diuresis, n=366 (25.5%); serum urea level, n=410 (28.5%); serum calcium level, n=201 (18,1%); serum phosphate level, n=411 (28.6%); calcium × phosphate product level, n=351 (24.4%); serum parathyroid hormone level, n=614 (42.7%); serum albumin level, n=240 (16.7%); serum hemoglobin level, n=244 (17.0%); quality of life (12-item short form health survey): physical component score, n=297 (20.7%); quality of life (12-item short form health survey): mental component score, n=297 (20.7%). HRQoL, health-related quality of life; IQR, interquartile range; PTH, parathyroid hormone; SF-12, 12-item short form health survey.
[a]Including both conventional hemodialysis and hemodiafiltration.
[b]Calculated using CKD Epidemiology Collaboration 2021 eGFR equation.

Association between Pruritus and HRQoL

The PCS score at dialysis initiation was 36.0 (SD, 10.0) and the MCS score was 47.0 (SD, 10.1). Table 4 shows the association between pruritus on HRQoL. The presence of pruritus was associated with both lower physical and mental HRQoL (adjusted β=−2.04; 95% CI, −2.78 to −1.30 and adjusted β=−1.73; 95% CI, −2.51 to −0.94, respectively) compared with no pruritus. Receiving treatment for pruritus was not an effect modifier in the relation between pruritus and HRQoL (P = 0.278 and P = 0.812 for the interaction term in the models with physical HRQoL and mental HRQoL, respectively), meaning that the association between pruritus and physical or mental HRQoL did not differ between patients receiving antipruritic treatment and patients without treatment.

Sensitivity Analyses

In summary, all sensitivity analyses yielded results comparable with the main analyses, both for the association between treatment and pruritus severity and for the association between pruritus and HRQoL. The results of the sensitivity analyses are listed in Supplemental Tables 3, A and B and 4, A and B.

Discussion

We found a high prevalence of pruritus in the first year of dialysis, with more than half of the dialysis patients experiencing pruritus (ranging from 50% to 56%). Of those patients, the majority experienced fluctuating pruritus or persistent pruritus, with a prevalence around 42.3% and 33.4%, respectively. Only a quarter of the patients with pruritus received medical treatment with antipruritic agents during their first year of dialysis, with topical emollients being the most prevalent. Receiving topical treatment and combined treatment showed an association with more severe pruritus compared with no treatment. Within the

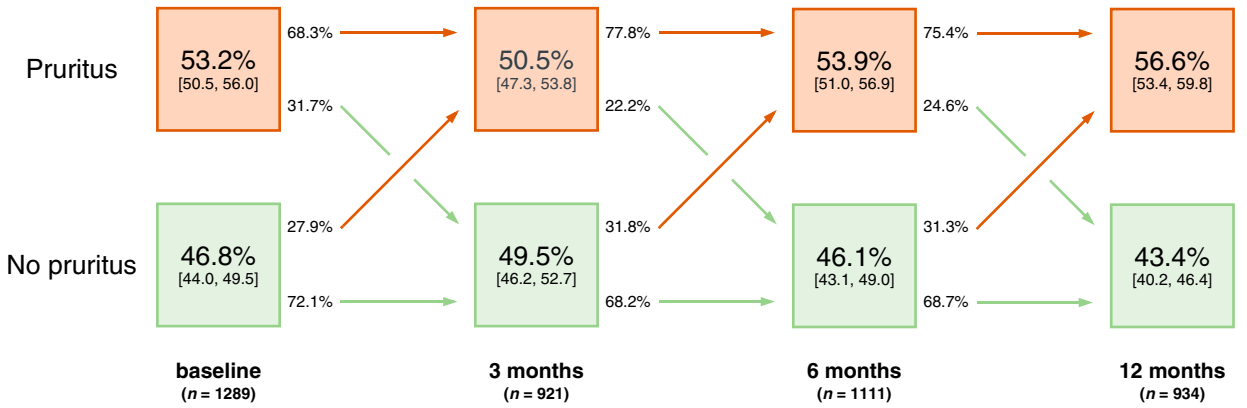

Figure 1. Prevalence and trajectory of pruritus in incident dialysis patients. The figure above shows the trajectory of pruritus. The prevalence is reported as a proportion with 95% CI. Arrows show the proportion of patients changing among groups. The percentages for changes apply only to patients with two consecutive measurements. Patients with missing data for either of the measurements are not included in these percentages. CI, confidence interval.

different medications used, emollients also showed an association with more severe pruritus compared with no treatment. Finally, pruritus was associated with lower physical and mental HRQoL. This association did not change if patients received treatment for their pruritus.

This study emphasizes that pruritus is common and impactful within the dialysis population, with over half of the patients experiencing pruritus in their first year of dialysis. Over the past years, varying prevalences have been reported by multiple studies, sometimes reaching up to 84% of patients reporting symptoms.[4,28] Two recent studies reported similar prevalences around 50%.[8,9] In contrast to one of those studies, we identified a lower percentage of patients with persistent pruritus. Approximately 70% of patients experienced persistent pruritus in this study, compared with the 42% we found.[8] This is in accordance with three other studies that reported percentages ranging from 22% to 59%.[9,28,29] By conducting multiple measurements within the first year, this study could differentiate between patients with persistent pruritus and those with fluctuating pruritus. Presumably, the longer intervals between measurements in the aforementioned studies may have resulted in reduced sensitivity to make that distinction, resulting in higher percentages of patients with persistent pruritus. The observation that pruritus presents itself persistently or intermittently illustrates the heterogeneous nature of pruritus. This, in turn, presents difficulties for physicians in developing individualized effective treatment options.

Despite the high prevalence of pruritus, only a small number of patients receive medical treatment. Similar proportions were found in a recent multinational study based on the Dialysis Outcomes and Practice Patterns

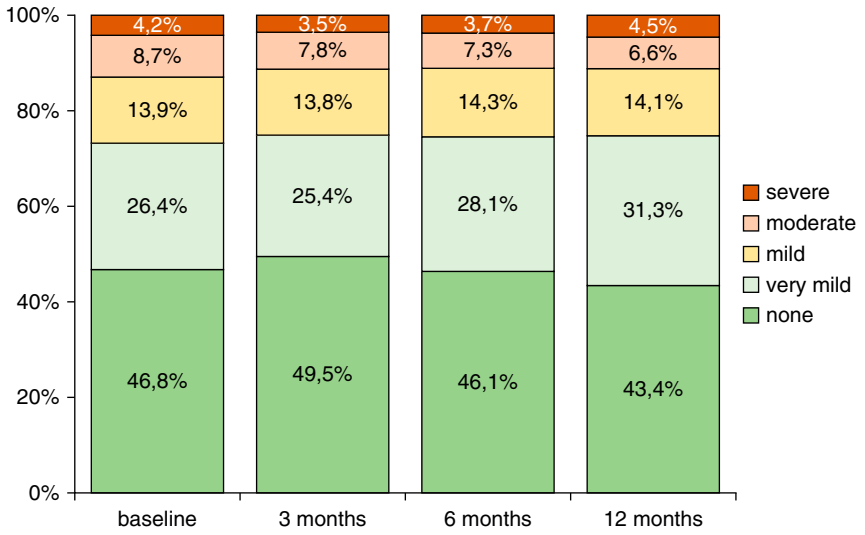

Figure 2. Severity of pruritus over time in incident dialysis patients. The graph above shows the severity of pruritus on a five-point Likert scale (ranging from none to severe) over time.

Table 2. Prescribed treatments with an antipruritic effect during the first year of dialysis

Treatment	Baseline (n=955)	3 mo (n=930)	6 mo (n=876)	12 mo (n=722)
Overall treatment, *n* (%)				
None	744 (77.9)	716 (77.0)	675 (77.1)	531 (73.5)
Topical	92 (9.6)	100 (10.8)	93 (10.6)	81 (11.2)
Systemic	90 (9.4)	89 (9.6)	77 (8.8)	79 (10.9)
Both	29 (3.0)	25 (2.7)	31 (3.5)	31 (4.2)
No. of medications, *n* (%)				
1	161 (16.9)	169 (18.2)	151 (17.2)	144 (19.9)
2	42 (4.4)	39 (4.2)	43 (4.9)	39 (5.4)
3	7 (0.7)	5 (0.5)	6 (0.7)	8 (1.1)
4	1 (0.1)	1 (0.1)	1 (0.1)	0 (0.0)
Topical treatment, *n* (%)				
Emollient	82 (8.6)	86 (9.2)	88 (10.0)	73 (10.1)
Levomenthol	4 (0.4)	3 (0.3)	1 (0.1)	3 (0.4)
Capsaicin	3 (0.3)	1 (0.1)	2 (0.2)	2 (0.3)
Calcineurin inhibitor	0 (0.0)	1 (0.1)	1 (0.1)	0 (0.0)
Topical corticosteroid	53 (5.5)	56 (6.0)	55 (6.3)	48 (6.6)
Systemic treatment, *n* (%)				
Antihistamine	58 (6.1)	59 (6.3)	56 (6.4)	48 (6.6)
Gabapentinoid	39 (4.1)	37 (4.0)	37 (4.2)	55 (7.6)
Serotonin receptor antagonist	12 (1.3)	4 (0.4)	3 (0.3)	0 (0.0)
SSRI	17 (1.8)	17 (1.8)	13 (1.5)	14 (1.9)
Leukotriene receptor antagonist	2 (0.2)	2 (0.2)	3 (0.3)	3 (0.4)

SSRI, selective serotonin reuptake inhibitor.

Study, with 68% of the patient not receiving medical treatment.[9] This is partly due to the fact that pruritus is not always diagnosed, with underestimation by treating physicians and underreporting by patients playing a role. A study from Rayner *et al*. states that the majority of health care providers estimate that <5% of patients suffer from pruritus, in contrast to the often-reported prevalence of 50%.[4] In addition, Lanot *et al*. describe that 37.6% of pruritus cases were only diagnosed through systematic screening, further emphasizing the importance of patient-reported outcome measures.[30] Rayner *et al*. also observed that treating physicians consider medication for pruritus the least important therapeutic option. This illustrates a second explanation for a low treatment percentage: there is great uncertainty regarding the efficacy of various agents and a lack of clear guidelines.[4]

Our study demonstrates that topical treatment, especially with emollients, was associated with more severe pruritus. There have only been a few studies on the effectiveness of emollients on pruritus, often of varying quality. Nevertheless, these studies show beneficial effects on dry skin, but inconsistent effects on pruritus itself.[31–33] We do not assume that emollients induce pruritus in dialysis patients. In fact, we ascribe the association we observed to indication bias: physicians are more likely to prescribe these agents to patients with more severe itching, which influences the association. Moreover, if the treatment would be very effective, we would have expected to find a negative association with severity, due to the longitudinal design of the study. One of the medications that often show a positive effect on pruritus are gabapentinoids. Several systematic reviews, that included both randomized controlled trials and observational studies, conclude that significant improvement in pruritus after treatment with either of these agents.[13,16,34] However, we found no association between the treatment with gabapentinoids and a reduction in pruritus compared with no treatment. Indication bias could play a role here as well, with patients experiencing severe refractory pruritus being prescribed gabapentinoids, resulting in an attenuation of any possible effectiveness of those gabapentinoids. These findings emphasize the necessity for thorough placebo-controlled trials to explore these possible effective treatments on a larger scale.

We observed a negative effect of pruritus on both physical and mental HRQoL. These findings align with previous studies, in which similar negative effects have been identified.[6–10] Some of these studies indicate that a proportion of this reduced HRQoL can be attributed to decreased sleep quality.[35,36] Although we did not observe a positive association between various treatments and the severity of pruritus, it is possible that some of these treatments may have a beneficial effect on HRQoL through alternative pathways, such as improving sleep quality. This could be the case, for example, with antihistamines and gabapentinoids, of which positive effects on sleep are known beyond itch relief.[37,38] However, treatment did not alter the association between pruritus and HRQoL. Presumably, this is partly due to the limited efficacy of the treatments on pruritus. In addition, it is plausible that the reduced HRQoL is not solely a result of diminished sleep, but that various other factors, such as an increase in depressive symptoms, also play a role.[5]

Table 3. Longitudinal effects of the treatment of pruritus on the severity of pruritus compared with no treatment during the first year of dialysis in incident dialysis patients

Treatment	Severity of Pruritus[a]					
	Unadjusted			Adjusted		
	Coefficient	95% CI	*P* Value	Coefficient	95% CI	*P* Value
Overall treatment[b]						
None	Ref[c]			Ref[c]		
Topical	0.36	0.21 to 0.51	<0.001	0.14	0.02 to 0.27	0.026
Systemic	0.14	−0.01 to 0.29	0.076	0.02	−0.10 to 0.14	0.730
Both	0.74	0.48 to 1.00	<0.001	0.36	0.16 to 0.57	<0.001
Topical treatment[d]						
None	Ref[c]			Ref[c]		
Emollient	0.47	0.25 to 0.67	<0.001	0.31	0.15 to 0.48	<0.001
Levomenthol	0.63	−0.78 to 2.04	0.381	0.63	−1.08 to 2.34	0.470
Capsaicin	0.26	−1.16 to 1.68	0.722	0.15	−1.06 to 1.35	0.811
Calcineurin inhibitor	0.02	−1.97 to 2.02	0.981	−0.12	−1.83 to 1.59	0.892
Topical corticosteroid	0.04	−0.21 to 0.30	0.739	−0.08	−0.29 to 0.13	0.450
Systemic treatment[e]						
None	Ref[c]			Ref[c]		
Antihistamine	0.28	0.04 to 0.51	0.022	0.15	−0.04 to 0.34	0.124
Gabapentinoid	−0.16	−0.40 to 0.08	0.196	−0.05	−0.24 to 0.14	0.613
Serotonin receptor antagonist	0.24	−0.34 to 0.82	0.418	−0.04	−0.52 to 0.44	0.880
SSRI	−0.15	−0.63 to 0.33	0.534	−0.17	−0.51 to 0.16	0.312
Leukotriene receptor antagonist	−0.52	−2.52 to 1.48	0.609	−0.21	−1.92 to 1.50	0.809

CI, confidence interval; SSRI, selective serotonin reuptake inhibitor.
[a]Severity of pruritus (scale 1–5).
[b]Adjusted for age, sex, modality at baseline pruritus associated comorbidity, severity of pruritus at baseline, dry skin at baseline, time.
[c]Reference category.
[d]c+systemic treatment.
[e]c+topical treatment.

This study has several strengths. It has a large prospective cohort with incident dialysis patients, to provide better insight in pruritus during the first year of dialysis. Furthermore, it has a relatively large proportion of peritoneal dialysis patients. Its longitudinal design with multiple repeated measures during follow-up provided a more

Table 4. Longitudinal effects of pruritus on HRQoL during the first year of dialysis and the influence of treatment for pruritus

Outcome Model	HRQoL Sum Score[a]		
	Coefficient	95% CI	*P* Value
Physical HRQoL			
Unadjusted	−1,97	−2.68 to −1.26	<0.001
Adjusted[b]	−2.04	−2.78 to −1.30	<0.001
Mental HRQoL			
Unadjusted	−1.59	−2.35 to −0.84	<0.001
Adjusted[b]	−1.73	−2.51 to −0.94	<0.001
Interaction between pruritus and treatment[c]			
Physical	NA[d]	NA[d]	0.278[e]
Mental	NA[d]	NA[d]	0.812[e]

CI, confidence interval; HRQoL, health-related quality of life.
[a]Ranging from 0 to 100.
[b]Adjusted for age, sex, modality, primary kidney disease, kidney transplantation in past, and time.
[c]Adjusted for age, sex, modality, primary kidney disease, kidney transplantation in past, and time with interaction with pruritus treatment.
[d]Not applicable.
[e]*P* value for interaction term.

detailed understanding of the trajectory of pruritus during the first year of dialysis. Its extensive data collection included detailed and repeated information on current treatment for pruritus, including both systemic and topical treatment. With the use of LMM, longitudinal associations could have been assessed and both between-patient and within-patient correlations were accounted for. Sensitivity analyses further ensured robustness of these results.

This study also has a few limitations. First, the results are based on observational research, making claims on causality relating treatment for pruritus difficult. And although the found associations give insight into the possible effect on pruritus, the actual causal effect remains hypothetical. Second, some of the included medications have multiple indications (*e.g.*, gabapentinoids for neuropathic pains and selective serotonin reuptake inhibitors for depression). This implies that it is imaginable that some patients have been prescribed the medications for a different indication. However, the indication does not affect the association between the treatment and pruritus. Third, previous studies have shown that ultraviolet phototherapy has potential beneficial effects on pruritus.[39,40] Unfortunately, information on ultraviolet therapy was not available in this study. Fourth, owing to the design of the study a distinction between patients on hemodialysis and on hemodiafiltration could not be made. It should be noted that the use of high-flux membranes is standard care in The Netherlands and Belgium. Fifth, the DSI questionnaire is not validated to assess pruritus in dialysis patients. However, the DSI scale shows similarities with the validated worst itching intensity numerical rating scale, the first being a scale from 1 to 5 and the latter being a scale from 0 to 10, both ranging from no pruritus to severe pruritus.[41] Therefore, we believe that the assessment of pruritus is sufficiently captured by the DSI. Finally, Kappa-opioid receptor antagonists with potential effects on pruritus have not been included in the current analysis.[42,43] They were approved by the European Medicines Agency in 2022, falling outside this study period. Future studies need to further assess these potential effects and the long-term outcomes of this new antipruritic agent.

In conclusion, pruritus is highly prevalent in the first year of dialysis, with only a small proportion of the patients with pruritus receiving treatment. These treatments are not associated with a relief of the burden of pruritus. Furthermore, this study demonstrates that pruritus has a negative effect on HRQoL, regardless whether patients receive treatment. Our findings highlight that it remains crucial for treating clinicians to be aware of the burden of pruritus in dialysis patient and to have well-established guidelines for the diagnosis and treatment of pruritus. Subsequently, there is a need for larger placebo-controlled randomized trials to investigate potentially effective treatments based on the identified pathophysiological mechanisms.

Disclosures

Disclosure forms, as provided by each author, are available with the online version of the article at http://links.lww.com/KN9/A732.

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Data Sharing Statement

Partial restrictions to the data and/or materials apply. The data that support the findings of this study are available from the corresponding author on reasonable request and with permission of the DOMESTICO steering committee.

Supplemental Material

This article contains the following supplemental material online at http://links.lww.com/KN9/A731.

Supplemental Table 1. STROBE statement.

Supplemental Table 2. Overview of treatments.

Supplemental Table 3. Sensitivity analyses of the effect of treatment on pruritus.

Supplemental Table 4. Sensitivity analyses of the effect of pruritus on health-related quality of life.

Supplemental Table 5. Participating centers and investigators.

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